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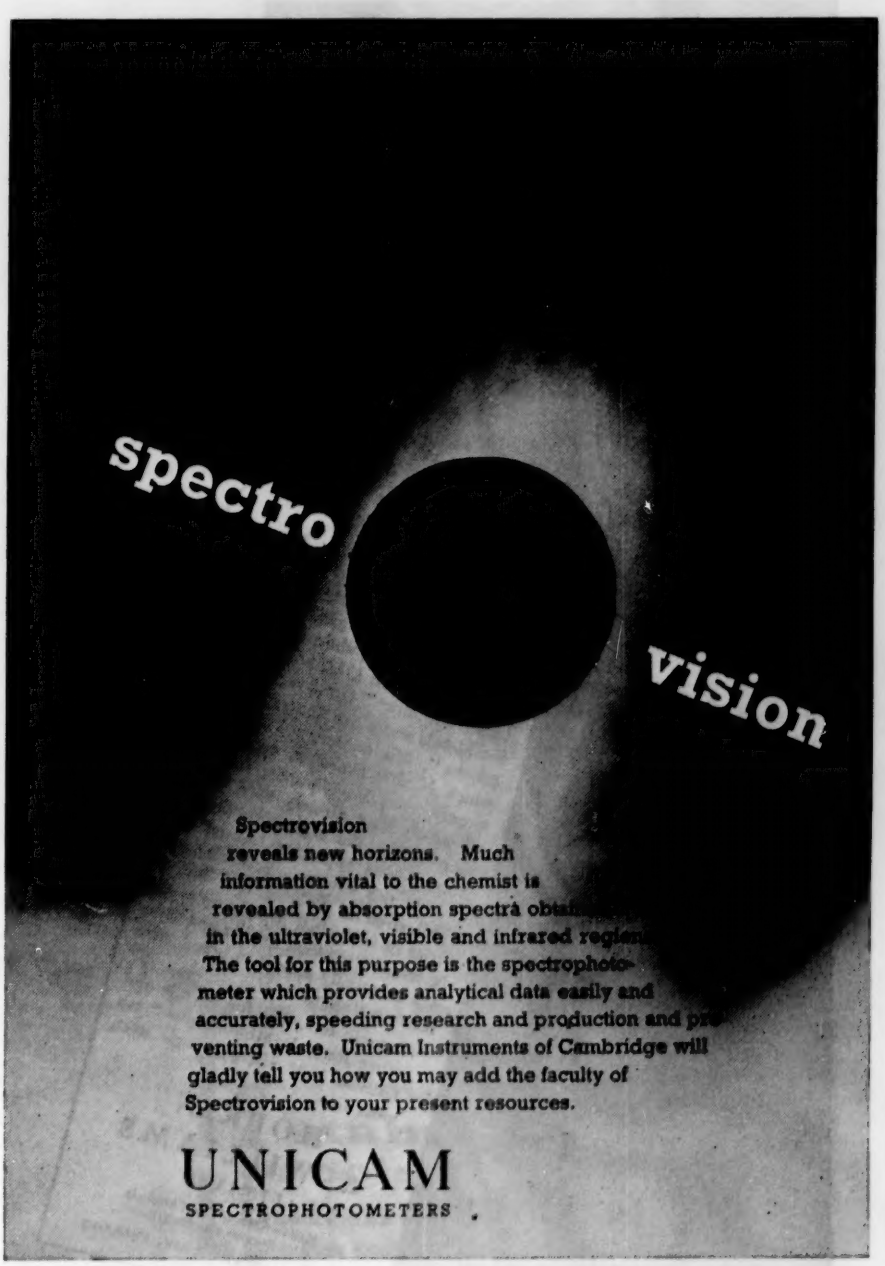
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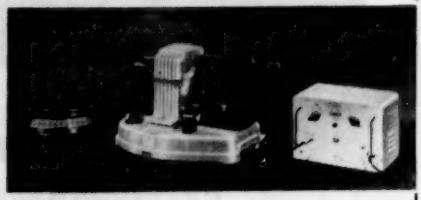

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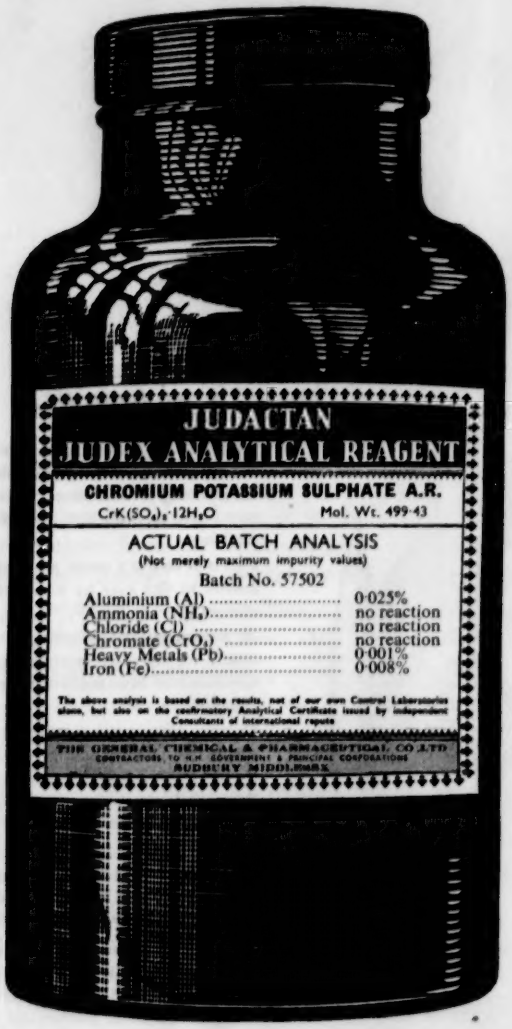
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The Kinetics of Hydrogen Isotope Exchange Reactions. Part II. The Reaction between* para-*Substituted* [*o*-^{2}H]*Phenols and Aqueous Sulphuric Acid.*

By V. Gold and D. P. N. Satchell.

[Reprint Order No. 6360.]

The loss of deuterium from *p*-nitro[*o*-^{2}H]phenol, *p*-chloro[*o*-^{2}H]phenol, and [*o*-^{2}H]*p*-cresol has been examined kinetically in various sulphuric acid–water mixtures. The logarithms of the rate constants of the reactions are found to vary linearly with Hammett's acidity function H_0, except at the highest acidities ($H_0 < -8$) where the rate increase is less steep.

The results are held to indicate that the rate-determining step of the exchange reaction is an intramolecular rearrangement of a conjugate acid of the phenol.

It is well established that the velocity of hydrogen isotope exchange between aromatic compounds and aqueous acid, under heterogeneous conditions, increases rapidly with the concentration of acid in the aqueous phase and, more generally, that the kinetic efficiency of acids is qualitatively related to their acidity (Ingold, Raisin, and Wilson, *Nature*, 1934, **134**, 734; *J.*, 1936, 915, 1637). The object of the present study was to examine the dependence of reaction velocity on acidity over a wider range, in a more quantitative fashion, in the hope of gaining a better insight into the mechanism of the reaction. In particular, it was thought at the outset that the acidity dependence might throw light on the nature and kinetic efficiency of the different acidic (H_3O^+, H_2SO_4, HSO_4^-, etc.) and basic (H_2O, HSO_4^-, SO_4^{2-}, etc.) species known to be present in sulphuric acid–water mixtures. Earlier two-phase experiments (Gold and Long, Part I*) on the exchange between [9-^{2}H$_1$]anthracene and sulphuric acid (84—90 wt.%) had indicated the promise of such an investigation, but the need for experiments on the distribution of the organic substrate between the two phases diminished the accuracy of the results and complicated their interpretation. For this reason single-phase experiments were adopted in the present work. In the event, experimental results provided diagnostic information about the mechanism of the reaction in a form different from that expected.

The choice of *para*-substituted phenols for this study was governed by practical considerations concerning properties such as solubility, basicity, exchange reactivity, and resistance to sulphonation or oxidation by sulphuric acid. Useful substrates must also have only one type of exchanging position if kinetic complexity is to be avoided. Some information about the exchange behaviour of *p*-nitrophenol was available (Koizumi and Titani, *Bull. Chem. Soc. Japan*, 1938, **13**, 318) which suggested appropriate experimental conditions for the preparation of *p*-nitrophenol deuterated practically exclusively at the position *ortho* to the hydroxyl group. Analogous information was not available in the cases of *p*-cresol and *p*-chlorophenol, but there was some evidence which implied that it would be possible to achieve selective exchange in these cases also (Kistiakowsky and Tichenor, *J. Amer. Chem. Soc.*, 1942, **64**, 2302; Tryon, Brown, and Kharasch, *ibid.*, 1948, **70**, 2003; Brodskii, *Izvest. Akad. Nauk S.S.S.R.*, 1949, 3).

The reaction rates studied all refer to dilute solutions of an aromatic compound in aqueous sulphuric acid. The reaction observed was the replacement of deuterium initially present in the aromatic compound by protium derived from a completely light solvent. Under these conditions the exchange kinetics assume a particularly simple form (Harris, *Trans. Faraday Soc.*, 1951, **47**, 716) and the greatest economy in the use of deuterium is achieved.

Experimental

Isotope Analysis.—The method used has been described by Bryce-Smith, Gold, and Satchell (*J.*, 1954, 2743). The percentages of deuterium are relative to the natural abundance of deuterium and are based on the assumption that the suppliers' (Norsk Hydro) analysis of

* Part I, *J. Amer. Chem. Soc.*, 1953, **75**, 4543.

99·73% D_2O was correct. A sample containing G% by weight of this commercial deuterium oxide and $(100 - G)$% by weight of laboratory distilled water is then described as containing 0·9973G% of D_2O by weight. All the analyses reported were obtained by comparison with the densities of standard samples prepared in this manner. A more rigorous expression of the analytical figures is unnecessary for our present purpose. Atom percentages ($\equiv 100F$) were calculated from these weight percentages (W) by the expression

$$\text{Atom percentage} = 100W/[W + 1{\cdot}1111(100 - W)]$$

Solvents.—The concentrations of the sulphuric acid–water mixtures were determined by titration and/or density measurements.

Experiments on the Preparation of ortho-*Deuterated Phenols.*—All the deuterated specimens were prepared by direct substitution, an enriched acid being used. This method depends on the directional properties of the substituents already present in the molecule. Since the products, unlike those from other aromatic substitution reactions, cannot be freed from unwanted isomers, great care has to be taken in the choice of experimental conditions in order to avoid their formation. The following exploratory experiments indicated that suitable conditions could be found for our compounds. The deuterium oxide sample used in them contained 99·7% of D_2O.

(a) p-*Nitrophenol.* The behaviour of *p*-nitrophenol in acid solution was examined by heating samples of " enriched " perchloric acid [60·0% perchloric acid (2·96 g.) together with deuterium oxide (0·0877 g.)] with a comparable amount of *p*-nitrophenol (1·20 g.) in sealed ampoules at 100°. At intervals the ampoules were cooled and opened, their contents were diluted with a little distilled water, and the solid nitrophenol was filtered off. This was recrystallised from water in such a way as to remove deuterium from the hydroxyl group without disturbing the deuterium atom attached to the nucleus. The admissibility of this procedure follows from Koizumi and Titani's experiments (*loc. cit.*). The nitrophenol was then subjected to isotopic analysis with the following results:

Duration of expt. (hr.)	70	140	190	430	1100
Wt. % of D_2O in combustion water	2·07	2·03	2·07	2·07	2·11

These figures indicate that the amount of deuterium taken up by the compound had reached a constant value after <70 hr. The deuterium percentage is consistent with the assumption that two nuclear hydrogen atoms (in addition to the hydroxylic hydrogen) are concerned in the exchange and that the partition ratio (ρ_{O-H}) for the deuterium exchange between nuclear hydrogen and perchloric acid

$$\rho_{O-H} = \frac{\text{Atoms \% D in C–H bonds of nitrophenol}}{\text{Atoms \% D in aqueous perchloric acid}}$$

has a value of $0{\cdot}98_8 \pm 0{\cdot}01$ at 100°. This value agrees with other determinations of distribution coefficients for similar exchange equilibria (cf. Gold and Satchell, *Quart. Rev.*, 1955, **9**, 51). In this calculation of ρ_{O-H} we used the result of a separate experiment which showed that the corresponding constant for the O–H bond in *p*-nitrophenol (ρ_{O-H}) had a value of 1·06 (cf. Koizumi and Titani, *loc. cit.*). It seems legitimate to assume that the two nuclear positions concerned in the exchange are those *ortho* to the hydroxyl group and that, under the conditions stated, it is possible to prepare *p*-nitro[*o*-^{2}H]phenol with a suitable content of deuterium and essentially free from deuterium in the *meta*-positions.

The main batch of material was accordingly prepared by this method [*p*-nitrophenol (40 g.), deuterium oxide (4 ml.), 60% perchloric acid (20 ml.) heated at 100° in a sealed glass flask for 100 hr]. After several crystallisations from water the specimen contained 6·00 atoms % of D. This sample was used in all the kinetic experiments with this compound.

(b) p-*Chlorophenol.* An exploratory experiment was carried out at 100°. Sealed ampoules each containing 60·0% perchloric acid (37·37 g.), deuterium oxide (0·801 g.), and *p*-chlorophenol (1·20 g.) were heated to 100°. After an appropriate length of time an ampoule was cooled and opened, and its contents diluted with water and extracted with ether. The ethereal extract was shaken with barium carbonate to remove any acid, and then dried ($MgSO_4$). After filtration the ether was removed by evaporation under reduced pressure. The residue was redissolved in sufficient water to free the hydroxyl group from detectable deuterium. This aqueous solution was again extracted with ether, the ethereal extract dried, and the ether removed as before. The residue was distilled rapidly in a semimicro-apparatus. This procedure was adopted in

order to minimise possible errors arising from isotope exchange between the hydroxyl group and the nucleus at high temperatures. The occurrence of such a reaction was reported for phen[^{2}H]ol at 200° (Brodskii and Kukhtenko, *Dopovidi Akad. Nauk Ukrain.*, 1950, 279) and, for this reason, prolonged heating of the substance was avoided. The only distillation in the above procedure occurred in the final stage immediately before combustion, at which stage this type of exchange reaction should be of no consequence. The results were :

Duration of expt. (hr.)	24	70	90
Wt. % of D_2O in combustion water	2·00	2·53	2·60

These figures correspond to an increasing number of nuclear hydrogen atoms being involved in the exchange. If the values of ρ for the C–H and O–H bonds of this compound are assumed to be similar to those found for *p*-nitrophenol, the lowest value corresponds to an average participation of about 2·3 and the highest value to about 3·0 nuclear hydrogen atoms per molecule. It is therefore apparent that the positions *ortho* to the hydroxyl group, which are expected to be the most reactive, are not the only positions involved in the exchange under these conditions. It was therefore attempted to discover conditions for more selective substitution. An experiment, by the same procedure, was carried out at 25° with *p*-chlorophenol (0·80 g.), 73·81 wt.% sulphuric acid (182·0 g.), and deuterium oxide (2·20 g.) in each ampoule :

Duration of expt. (hr.)	16	40	64
Wt. % of D_2O in combustion water	1·06	1·16	1·16

The last two figures correspond to the occurrence of exchange at exactly two positions (as desired) if ρ_{O-H} has a value of $0{\cdot}98_6$.

Because of the low solubility of *p*-chlorophenol in acid, the main batch of material was prepared by a two-phase process in which *p*-chlorophenol (50 g.) in carbon tetrachloride (50 ml.) was shaken (40 hr. at 20°) with sulphuric acid (200 ml., 80% by wt.) and deuterium oxide (12 ml.). The time of shaking was selected by consideration of the volumes of the phases and the distribution of *p*-chlorophenol between them. The figures for the deuterium content, given below, show that exchange equilibrium was not reached even at two nuclear positions, and the product may therefore be considered to be reasonably free from *p*-chloro[*o*, *m*-^{2}H]-phenol. After separation of the phases, the carbon tetrachloride layer was shaken several times with water and then dried ($MgSO_4$). The carbon tetrachloride was distilled off under reduced pressure. The residue crystallised. It was considered inadvisable to subject the sample to distillation in case an isotope rearrangement occurred. The chief impurity likely in the sample is a trace of carbon tetrachloride, which is of no consequence in the isotope assay or the kinetic exchange experiments. The specimen contained 2·98 atoms % of D.

(c) p-*Cresol*. The investigation concerning the preparation of [*o*-^{2}H]*p*-cresol proceeded along lines similar to those described for *p*-chlorophenol. A high-temperature (100°), one-phase experiments, using *p*-cresol (1·00 g.), perchloric acid (60 %; 37·37 g.), and deuterium oxide (0·801 g.) per ampoule and a separation technique similar to that used in the corresponding experiment with *p*-chlorophenol, showed an increasing amount of deuterium uptake by the aromatic compound with time :

Duration of expt. (hr.)	24	70	90
Wt. % of D_2O in combustion water	1·52	1·94	2·00

These figures indicate the average participation of 2·9—3·8 hydrogen atoms per molecule, and show that the experimental conditions are two drastic. In a low-temperature (25°), one-phase experiment, using *p*-cresol (0·80 g.), perchloric acid (60%, 123·2 g.), and deuterium oxide (2·20 g.) per ampoule, it was possible to confine isotope equilibration to two positions :

Duration of expt. (hr.)	1	24	48
Wt. % of D_2O in combustion water	0·90	0·91	0·93

These figures are consistent with the effective participation of 2·00, 2·02, and 2·05 nuclear positions, respectively, if the value of ρ_{O-H} is assumed to be $0{\cdot}95_2$.

The main batch of *p*-cresol was deuterated in a two-phase experiment. *p*-Cresol (40 g.), in carbon tetrachloride (30 ml.), was shaken (10 hr., 20°) with perchloric acid (60%; 200 ml.) and deuterium oxide (25 ml.). The product was isolated by the route described for *p*-chlorophenol. Analysis showed that exchange equilibrium was by no means reached even at the positions *ortho* to the hydroxyl group. The total hydrogen in the product contained 2·56 atoms % of D.

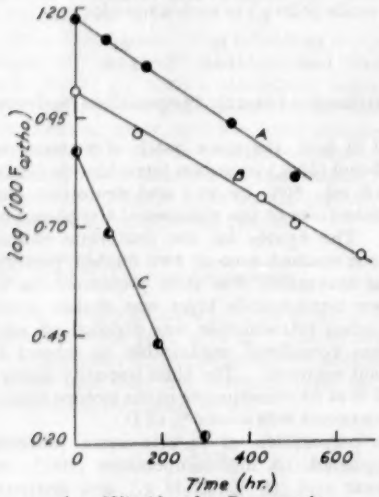
Kinetic Experiments on the Loss of Deuterium from the ortho-*Positions.*—Samples of the deuterated phenols (0·6 g.) were dissolved in portions of sulphuric acid (220 ml.) contained in flasks which were then sealed off and kept at 25° (thermostat). After various time intervals the flasks were removed and opened. Their contents, after dilution with water when necessary (the temperature being kept below 25°), were extracted with ether. The extract was kept over barium carbonate and anhydrous magnesium sulphate for several hours, then filtered, and the ether distilled off. The residual *p*-nitrophenol was analysed without further treatment; *p*-cresol and *p*-chlorophenol were first distilled to free them from the last traces of ether.

The percentage of deuterium in the system being so small, the exchange kinetics should not deviate detectably from first-order behaviour (Harris, *loc. cit.*) and should obey a relation of the form

$$\ln (F_0/F) = \lambda t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

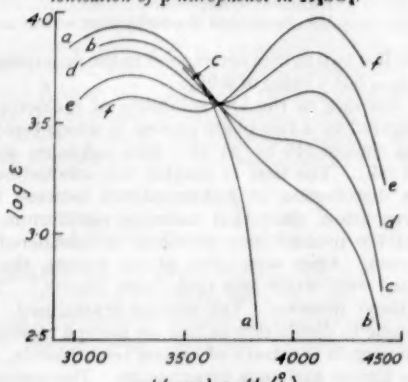
where F_0 and F are the fractional abundances of deuterium present initially and after a time t respectively. This was found to be the case, and examples of the plots of log (F_0/F) against t

FIG. 1. *Examples of first-order exchange behaviour.*



A, p-*Nitrophenol*; *B*, p-*cresol*; *C*, p-*chlorophenol*.

FIG. 2. *Absorption spectra illustrating basic ionisation of* p-*nitrophenol in* H_2SO_4.



Concn. of H_2SO_4: *a*, 5; *b*, 89·62; *c*, 92·22; *d*, 94·52; *e*, 96·25; *f*, 98% by wt.

obtained for the three compounds are shown in Fig. 1. The linearity of these graphs serves to confirm that all the deuterium atoms in the samples occupy kinetically equivalent positions.

In experiments with *p*-nitrophenol in sulphuric acid of concentration greater than 50 moles %, when sulphonation might be expected, the rate of sulphonation was always small compared with that of exchange. In all cases the amount of phenol recovered was greater than 60% of the amount used. Therefore, errors which might result from selective sulphonation caused by the isotope effect on the reaction velocity of that reaction (Berglund-Larsson and Melander, *Arkiv Kemi*, 1953, **6**, 219) are considered to be negligible.

Basic Ionisation Constant of p-*Nitrophenol.*—Solutions of *p*-nitrophenol in concentrated sulphuric acid have a marked yellow-green colour which is removed on dilution. This suggests a basic ionisation of the nitro-group similar to that found in other nitro-compounds (cf. Brand, Horning, and Thornley, *J.*, 1952, 1374). By using spectrophotometric methods essentially similar to those described by Brand *et al.*, and a series of five acids in the 90—98 wt.% region, the extinction coefficient and the pK_a values for the conjugate acid of *p*-nitrophenol were determined (see Fig. 2):

$$\varepsilon_{max.} = 15{,}430 \text{ (4100 Å)}; \quad -pK_a = 9{\cdot}06$$

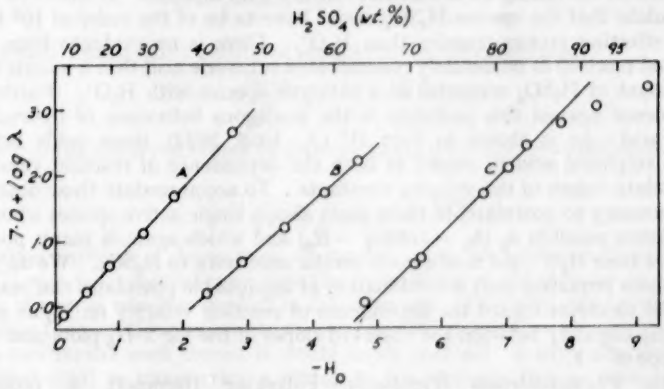
In calculating the exchange rate constant it was assumed, as seems reasonable, that the fraction of the phenol present as its conjugate acid did not undergo exchange. These rate

constants are therefore maximum values for the un-ionised phenol. No such ionisation is considered likely for the other two compounds. In these cases, too, the quoted rate constants are considered to apply to the un-ionised phenol.

Results and Discussion.

Dependence of Reaction Velocity on Acid Composition.—The kinetic results are tabulated below, and their dependence on acidity is shown in Fig. 3. It is seen that, over a considerable range of acidities (covering ~8 logarithmic units of acidity), log λ is a linear function

Fig. 3. *Dependence of exchange rate on acidity.*



A, p-*Cresol*; *B*, p-*chlorophenol*; C, p-*nitrophenol*.

of Hammett's acidity function H_0. The slopes of these graphs are 1·08, 0·90, and *ca.* 0·94 for *p*-cresol, *p*-chlorophenol, and *p*-nitrophenol respectively.

H_2SO_4 (wt. %)	$-H_0$	$10^7\lambda$ (sec.$^{-1}$) *p*-C_6H_4Me·OH	$10^7\lambda$ (sec.$^{-1}$) *p*-C_6H_4Cl·OH	H_2SO_4 (wt. %)	$-H_0$	$10^7\lambda$ (sec.$^{-1}$) *p*-$C_6H_4(NO_2)$·OH
9·8	0·15	0·61	—	64·3	4·80	1·16
14·5	0·50	1·73	—	70·3	5·58	4·40
19·3	0·85	4·00	—	71·1	5·68	5·33
27·0	1·35	13·3	—	78·8	6·65	48·5
34·5	1·85	47·0	—	81·3	7·03	123·0
40·5	2·36	—	1·57	82·9	7·31	270
45·3	2·75	438·3	—	87·2	7·85	508
47·0	2·90	—	4·73	92·2	8·40	1012
53·0	3·56	—	15·9	97·6	9·17	1933
59·0	4·18	—	53·2			
63·5	4·69	—	159·0			

As previously mentioned, an alternative method of analysis of the data was *ca.* also attempted in terms of the concentrations of the different Brönsted acids present in aqueous sulphuric acid, the absence of strong kinetic effects due to the medium being assumed, *i.e.*, on the basis of a rate equation of the form

$$(1/t) \ln (F_0/F) = \Sigma k_i A_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where F_0 and F have the same meaning as in equation (1) and A_i represents the concentration of the *i*th Brönsted acid in the system. The concentrations of the acidic species have been deduced from the intensities of Raman spectra of aqueous sulphuric acid (Young, *Record of Chem. Progress*, Spring Issue, 1951, p. 81, and personal communication). The concentrations of H_3O^+ and HSO_4^- are appreciable and reasonably well known over the acidity range with which we are concerned. It is evident from the data that the rate at which these concentrations increase with the stoicheiometric concentration of sulphuric

acid in the medium is far smaller than the corresponding increase in the reaction velocity. If, therefore, equation (2) were to describe the dependence of the exchange rate on the acid composition, the terms involving H_3O^+ and HSO_4^- cannot make a very significant contribution to the reaction velocity. The data concerning the concentration of the species H_2SO_4 refer only to the highest stoicheiometric concentrations and, on the basis of the Raman spectra, $[H_2SO_4]$ is indistinguishable from zero if the stoicheiometric concentration is less than 14M (80 wt. %). It would therefore be consistent with these data to postulate that, at any rate over most of the range, H_2SO_4 is, in fact, the only species which gives rise to a significant term in equation (2) and that its concentration decreases from the measured value of 3M at $[H_2SO_4]_{stoich.} = 15{\cdot}18$M to about 10^{-7}M at $[H_2SO_4]_{stoich.} = 1{\cdot}2$M, in such a way as to parallel the falling off in reaction velocity with dilution. It would be a corollary of this postulate that the species H_2SO_4 would have to be of the order of 10^8 times more reactive in effecting proton transfer than H_3O^+. There is no evidence from any other acid-catalysed reaction in moderately concentrated sulphuric acid that a minute and highly reactive amount of H_2SO_4 competes as a catalytic species with H_3O^+. Further circumstantial evidence against this postulate is the analogous behaviour of hydrochloric and phosphoric acid. As is shown in Part IV (*J.*, 1955, 3622), these acids behave very similarly to sulphuric acid in regard to both the dependence of reaction velocity on H_0 and the absolute values of the velocity constants. To accommodate these observations it would be necessary to postulate, in these cases also, a single active species whose decrease in concentration parallels h_0 (h_0 = antilog $-H_0$) and which again is many powers of 10 more reactive than H_3O^+, yet is of closely similar reactivity to H_2SO_4. We do not believe that an analysis requiring such a combination of improbable postulates can reasonably be defended and therefore regard the dependence of reaction velocity on H_0 as established, in spite of the disparity between the observed slopes of the log λ–H_0 plots and the ideally expected slope of -1.

Acid–Base Pre-equilibrium Hypothesis.—Following Hammett, a proportionality between a rate constant and h_0 has usually been interpreted as implying a rate-determining reaction of the conjugate acid of a substrate (either a unimolecular reaction or a bimolecular reaction with a second substance other than water), the initial protonation occurring rapidly and only to a small extent, *e.g.*:

$$HA + S \underset{}{\overset{\text{Fast}}{\rightleftharpoons}} SH^+ + A^-$$

$$SH^+ + \cdots \xrightarrow{\text{Slow}} \text{Products}$$

In applying this idea to the loss of deuterium from a substrate in an acidic medium we must be careful to note that we cannot identify SH^+ with a species (I) in which the entering hydrogen and the leaving deuterium atom occupy equivalent positions. This intermediate is the obvious one to formulate by analogy with the intermediates thought to occur in other electrophilic aromatic substitution reactions (Melander, *Arkiv Kemi*, 1950, **2**, 213; Ingold, "Structure and Mechanism in Organic Chemistry," Bell and Son, Ltd., London, 1953, pp. 279—281). If SH^+ were identical with (I), the rate law would require a dependence of reaction velocity on acidity analogous to that required by equation (2) [cf. equation (32) given by Gold and Satchell, *loc. cit.*], and this has already been dismissed as inconsistent with the observed dependence on H_0.

(I)

For this reason, if we accept the basic principles of the Hammett interpretation, we must identify SH^+ with a conjugate acid of the aromatic molecule of a structure such that the added proton does not occupy an equivalent position to the deuterium nucleus to be replaced. The entering hydrogen must (i) be linked less tightly than the deuterium to the carbon atom at which substitution occurs, or, (ii) be attached elsewhere in the same molecule, or (iii) be attached to a different phenol molecule from the one undergoing deuterium loss.

Intermolecular Mechanism.—The third of these possibilities would arise if a conjugate acid of the phenol (formed, say, by proton attachment at the oxygen atom) were to be the only acidic species effective in attacking the deuterium-carrying nucleus. Writing RD

and RH for the deuterated and light phenol molecules and ϕ for the phenol irrespective of its isotopic composition (*i.e.*, $[\phi] = [RH] + [RD]$), we can represent this mechanism as :

$$\phi + H_3O^+ \rightleftharpoons \phi H^+ + H_2O \text{ (Equilibrium constant } = K_a^{\phi H^+})$$

$$\phi H^+ + RD \underset{k_-}{\overset{k_+}{\rightleftharpoons}} RDH^+ + \phi \xrightarrow{k'_-} RH + \phi D^+$$

where RDH^+ stands for the conjugate acid of structure (I), and ϕD^+ and ϕH^+ are conjugate acids in which the hydrion attachment is of the looser kind mentioned above. This mechanism leads to the rate law

$$\lambda = \frac{k_+ \cdot k'_-}{k_- + k'_-}[\phi H^+] \cdot \frac{f_{\phi H^+} f_{RD}}{f_{(\phi \cdots H \cdots RD)^+}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Since for a small extent of conversion of phenol into its conjugate acid

$$\frac{[\phi H^+]}{[\phi]} = \frac{h_0}{K_a^{\phi H^+}} \cdot \frac{f_\phi f_{BH^+}}{f_{\phi H^+} f_B} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $K_a^{\phi H^+}$ is the acidity constant of ϕH^+, we have, if the activity coefficient ratio is unity

$$\lambda = \frac{k_+ k'_-}{(k_- + k'_-) K_a^{\phi H^+}} \cdot h_0[\phi] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

This equation involves a dependence of reaction rate on acidity compatible with our results. It was not practicable to test the dependence of the velocity on the total concentration of phenol which is implied in this equation. However, the following considerations lead us to reject this mechanism on quite general grounds.

If this mechanism were correct it would imply that ϕH^+ is more effective than H_3O^+ (or any other acid) in transferring a proton to the aromatic ring to form the conjugate acid (I). Let us consider the equilibrium between RH and its conjugate acid RH_2^+ which has the same structure as (I). We may reasonably assume that the basicities of RH and RD are the same. If the only acidic and basic species present in the system are ϕ, ϕH^+, RH_2^+, H_3O^+, and H_2O, the following conditions of equilibrium must obtain :

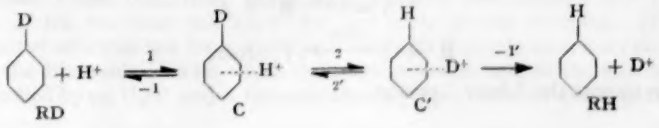
$$\frac{[RH_2^+]}{[RH]} = \frac{k_+^{H_3O^+}[H_3O^+]}{k_-^{H_3O}[H_2O]} = \frac{k_+^{\phi H^+}[\phi H^+]}{k_-^{\phi}[\phi]} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and

$$\frac{[RH_2^+]}{[RH]} = \frac{(k_+^{H_3O^+}[H_3O^+] + k_+^{\phi H^+}[\phi H^+])}{(k_-^{H_3O}[H_2O] + k_-^{\phi}[\phi])} \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The equations (6) follow from the condition that each of the acid–base pairs must separately be in equilibrium with the pair RH_2^+, RH. Equation (7) is a consequence of the requirement that, at equilibrium, the rate of attachment of a proton, from whatever source, to RH must equal the total rate of detachment. It follows that, if the acid ϕH^+ is, in preference to H_3O^+, responsible for most of the reaction converting RH into RH_2^+ then its conjugate base ϕ must be responsible for an equal share of the reverse reaction. Therefore, it would be necessary to say that ϕ is more effective than H_2O for proton (and deuteron) abstraction, in spite of the fact that H_2O is a stronger base and present in much greater concentration. For this reason, the intermolecular mechanism appears untenable and we have to consider that the initial proton attachment occurs in the molecule which subsequently loses deuterium—the slow step being intramolecular.

Intramolecular Mechanism.—On this basis we formulate the reaction mechanism as involving a rapid, reversible, loose attachment of a proton to the deuterated molecule which is then followed by a slow rearrangement of this species :



We may write the reaction velocities of the various steps in the form $v = k \times$ (activity of the organic species/activity coefficient of the transition state), so that the specific reaction rates k are functions of the solvent acidity. Assuming the concentrations of C and C′ to be very small, and applying Bodenstein's " stationary state " treatment, we obtain for the overall rate constant λ an expression of the approximate form

$$\lambda = \frac{k'_{-1}k_1k_2}{(k_{-1}k'_2 + k_{-1}k'_{-1} + k'_{-1}k_2)} \cdot \frac{f_{RD}}{f_{X^+}} \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

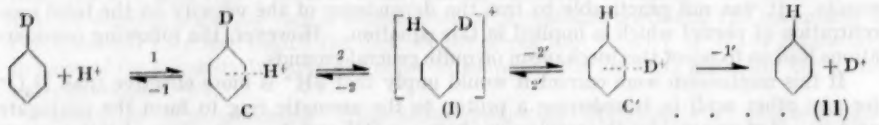
and, if $k'_{-1} \gg k'_2$ and $k_{-1} \gg k_2$,

$$\lambda = k_1k_2f_{RD}/k_{-1}f_{X^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

or

$$\lambda = h_0k_2(f_{RD}f_{BH^+})/K_a^C(f_{X^+}f_B) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where K_a^C is the acidity constant of C and hence $[C]/[RD] = k_1f_{RD}/k_{-1}f_C = h_0f_{RD}f_{BH^+}/K_a^Cf_Cf_B$. Equation (10) correctly represents the proportionality of the reaction rate to h_0 (on making the usual assumption that $f_{RD}f_{BH^+}/f_{X^+}f_B = 1$) and appears to be the simplest interpretation of this observation in accordance with Hammett's principle mentioned. However, by analogy with the case of aromatic nitration we consider it likely that the hydrogen isotope exchange also involves an intermediate of structure (I) and, for this reason, we prefer to formulate the reaction mechanism as :



(11)

where C and C′ and (I) are low-concentration intermediates. On this basis the expression for λ analogous to (8) becomes :

$$\lambda = \frac{k_1k'_{-1}k_2k'_{-2}}{k_{-1}k'_{-1}k'_{-2} + k_{-1}k'_{-1}k_2 + k'_{-1}k_2k'_{-2} + k_{-1}k_{-2}k'_2} \cdot \frac{f_{RD}}{f_{X^+}} \quad . \quad . \quad . \quad (12)$$

or, if k_{-1} and k'_{-1} are very much greater than the other k values,

$$\lambda = \frac{k_1}{k_{-1}} \cdot k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot \frac{f_{RD}}{f_{X^+}}$$

$$= \frac{h_0}{K_a^C} \cdot k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot \frac{f_{RD}f_{BH^+}}{f_{X^+}f_B} \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

which is identical with equation (10) except for the numerical factor $k'_{-2}/(k_{-2} + k'_{-2})$, the value of which is expected to lie in the range 0·09—0·33 (Gold and Satchell, *loc. cit.*). A comparison of the rate of deuterium and tritium loss from RD and RT may afford a test for the existence of an intermediate of structure (I) in these exchange reactions.

Examination of the Acid-freer Proton Pre-equilibrium Hypothesis.—Recently, during a discussion of the mechanism of hydration of olefins (de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930), a more general formulation of this type of mechanism was proposed. This formulation envisages a rapid equilibrium between acidic species and protons in a " freer form." The rate-determining step is the reaction between the protons and the substrate, *e.g.*,

$$HA \overset{\text{Fast}}{\rightleftharpoons} \mathbf{H}^+ + A^-$$

$$\mathbf{H}^+ + S \xrightarrow{\text{Slow}} \text{Products}$$

where $\mathbf{H}^+$ represents the " freer " proton.

The difference between such a description of the mechanism and that given in equation (11) is that the structurally less specific " freer " protons replace the conjugate acids C and C′ as reaction intermediates. If the proton is attached, however loosely, to S, then the two formulations are indistinguishable and, in our case, the " freer " proton is the proton attached to the aromatic molecule, in the complex C (or C′). If, on the other hand, the " freer " protons are not associated with the particular molecule undergoing exchange then, strictly speaking, the mechanism is chemically different, although a distinguishing experimental test has not yet been devised. For the hydrogen isotope exchange reaction the " freer " proton formulation can be written :

$$H_3O^+ \text{ (or } H_2SO_4) \underset{-1}{\overset{1}{\rightleftharpoons}} H_2O \text{ (or } HSO_4^-) + \mathbf{H}^+ \quad \text{(fast)}$$

$$RD + \mathbf{H}^+ \underset{-2}{\overset{2}{\rightleftharpoons}} RDH^+ \xrightarrow{-2'} RH + \mathbf{D}^+$$

$$\mathbf{D}^+ + H_2O \text{ (or } HSO_4^-) \underset{1'}{\overset{-1'}{\rightleftharpoons}} H_2DO^+ \text{ (or } HDSO_4) \quad \text{(fast)}$$

On this basis

$$\lambda = k_2 \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot (\mathbf{H}^+) \cdot \frac{f_{RD}}{f_{X^+}} \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where X^+ is the transition state of reaction (2), or, since $(\mathbf{H}^+) = \mathbf{K}(H^+)$ and $(H^+) = h_0 f_{BH^+}/f_B$,

$$\lambda = k_2\mathbf{K} \cdot \frac{k'_{-2}}{k_{-2} + k'_{-2}} \cdot h_0 \cdot \frac{f_{RD} f_{BH^+}}{f_{X^+} f_B} \quad . \quad . \quad . \quad . \quad . \quad (15)$$

which is formally identical with (13).

The experimental results of the present study are compatible with any type of " freer proton." However, the following discussion, during which the term " freer protons " is taken to refer to those " freer protons " which exist in some state *other* than that of a loose attachment to the reacting molecule, seems to us to argue against their kinetic intervention and that, therefore, it is justifiable to represent the reaction mechanism by the specific picture proposed in the preceding section.

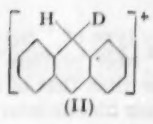
It is known that certain reactions exhibit general acid catalysis in dilute aqueous solution, *i.e.*, the total rates of these reactions can be satisfactorily represented as a sum of the contributions of catalysis by several acid species which are simultaneously present in the solvent. An example of this is the iodination of acetone. The detailed mechanism of this reaction is thought to be complex (cf. Bell, " Acid–Base Catalysis," Oxford, 1941, Chapter VII) but, for this additivity to hold, it must be true that the rate of proton uptake by acetone is the sum of the contributions to the velocity of this reaction by the individual acids. This must mean that these acids *directly* transfer protons to acetone and do not, in a pre-equilibrium, liberate " freer " protons which are then taken up by acetone, since the existence of such a pre-equilibrium is incompatible with additive catalytic effects. [This can be shown by an argument analogous to that which demonstrates that a reaction which exhibits general acid catalysis must involve a rate-determining proton transfer and cannot involve an acid–base pre-equilibrium of the reacting substrate (*idem*, *op. cit.*, pp. 122—127).] It follows that the reaction of any " freer protons " present with acetone must be less important than that of H_3O^+ ions and other acidic species. [The phenomenon of the simultaneous operation of proton transfer from different acids is also shown in a more direct manner in the exchange reaction between phosphine and water, although the data in this case are not as extensive as for the example quoted above (Weston and Bigeleisen, *J. Amer. Chem. Soc.*, 1954, **76**, 3074).] We may also suppose that this order of importance of the reactions will apply for any other proton acceptor. (The validity of the Brönsted catalysis law for a variety of reactions supports such a supposition.) On going from the dilute solutions for which the acetone results hold to the least acidic of the solutions studied by us, $^{T}H_3O^+$ and h_0 increase almost proportionately and it is expected that

(H^+) is nearly proportional to h_0. Therefore, we may expect that the relative importance of the reaction *via* " freer " protons and H_3O^+ ions will still be of the same order, the former reaction still being insignificant compared with the latter. In other words, " freer " protons do not play a part in the reaction in the dilute acids and therefore this mechanism cannot be invoked to explain the dependence of reaction velocity on h_0 in that region of acidity. Nothing seems to be gained by postulating its emergence at higher acidities. As previously mentioned, we therefore interpret our results as pointing to the occurrence of what may be regarded as a slow intramolecular rearrangement.

Chemical Formulation of the Intermediate C.—On the basis of the experiments reported in this paper at least two formulations of C seem chemically plausible. Either the proton is attached to the oxygen atom of the hydroxyl group or else there is a less localised interaction between the proton and the aromatic molecule of a type variously described as an outer complex (Mulliken, *J. Phys. Chem.*, 1952, **56**, 801) or π-complex (Dewar, " Electronic Theory of Organic Chemistry," Oxford, 1949; Brown and Brady, *J. Amer. Chem. Soc.*, 1952, **74**, 3570). This problem is more fully discussed in Part III (following paper).

Dependence of Reaction Velocity on Acidity at the Highest Concentrations of Acid.—The linear relation between log λ and H_0 breaks down at high acidity for *p*-nitrophenol. The deviation is definitely outside the limits of experimental error. In calculating these points allowance was made for the protonation of the nitro-group of nitrophenol which becomes important in this region. It was assumed that this protonated species is completely unreactive. Our determination of the pK_a value for *p*-nitrophenol is unlikely to be in error by a sufficiently large amount to make any significant difference to the result.

The deviation from linearity may be due to one or more of several causes and we cannot decide definitely between them. One possible reason is the inadmissibility of the assumption which allows equation (12) to be simplified to yield equation (13). It is conceivable that at the highest acidities the loss of a proton from C and C′ is no longer very much faster than the other reactions in view of the decreasing concentration of active bases in that composition region. Under these conditions λ will depend less strongly on h_0 and, in the limiting case of high acidities when k_{-1} and k'_{-1} are very much smaller than the other k values in equation (12), it will become independent of solvent acidity. In support of this hypothesis we may adduce that a rate of proton loss which decreases with acidity was postulated by Gold and Long (*loc. cit.*) for the ion (II) although the two cases are not strictly comparable.



(II)

An alternative explanation of the phenomenon would be along the lines of the argument suggested for the decrease in nitration rate observed over a similar range of acidities. In particular, it has been suggested by Gillespie and Norton (*J.*, 1953, 971) that the decrease is in part due to deactivation of the aromatic compound by hydrogen-bonding between potentially basic parts of the molecule with an H_2SO_4 molecule. In the case of nitro-compounds this interaction would take place at the nitro-group and deactivate the aromatic ring by electrostatic induction. This explanation could clearly be extended to the exchange reaction of *p*-nitrophenol studied by us. A similar kind of interaction was probably envisaged by Brand, Horning, and Thornley (*loc. cit.*) who suggested that the freezing-point depression of sulphuric acid by trinitrotoluene (Gillespie, Hughes, and Ingold, *J.*, 1950, 2743) could conceivably be explained by solvation of the nitro-group.

We may definitely rule out as an explanation an application of the hypothesis that at the higher acidities H_0 does not reflect an activity of protons but an activity of the Lewis acid SO_3 (Lewis and Bigeleisen, *J. Amer. Chem. Soc.*, 1943, **65**, 1144), because such an effect, if real (see Coryell and Fox, *J. Inorg. Nuclear Chem.*, 1955, **1**, 119), would only assume importance at acidities higher than those studied by us.

King's College, Strand, W.C.2. [*Received, April 27th*, 1955.]

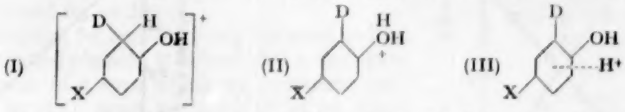
The Kinetics of Hydrogen Isotope Exchange Reactions. Part III. The Reaction between [$^2H_1$]Benzene and Aqueous Sulphuric Acid.*

By V. Gold and D. P. N. Satchell.

[Reprint Order No. 6361.]

The rate of loss of deuterium from [$^2H_1$]benzene in aqueous sulphuric acid solutions depends on the acidity of the solvent in a similar way to that for the analogous reactions of *ortho*-deuterated phenols. It is concluded that the exchange reactions of all those compounds proceed by a similar mechanism and involve a reaction intermediate in which the entering proton is more loosely attached to the aromatic nucleus than the departing deuteron. This conclusion is discussed with reference to related observations on the hydration of olefins, the basicity of aromatic hydrocarbons towards hydrochloric acid, and the general theory of aromatic substitution reactions.

The dependence of exchange velocity on solvent acidity in the reaction between deuterated phenols and sulphuric acid has been interpreted by us (Part II*) as requiring the postulation of an intermediate, the formula of which was that of a conjugate acid of the phenol. The structure of this intermediate was left undecided as a result of that work, the only kinetic requirement being a positional non-equivalence of the protium and deuterium nuclei which are involved in the exchange, *i.e.*, structure (I) was ruled out, but either (II) or (III) would be satisfactory as intermediates. In formula (II) the proton is attached to the phenolic oxygen



atom whereas the proton attachment in (III) is of a less definite character. We need not consider attachment of the proton to the group X as a separate possibility, since this is inherently improbable for the case of *p*-cresol (X = Me) which was one of the compounds studied by us. In order to decide whether the conclusions drawn by us from the previous work were to be restricted to molecules with a lone-pair donor atom adjacent to the ring, or whether they were of more general validity, it was necessary to examine the kinetic behaviour of a compound for which the formulation (II) was impossible, the somewhat different behaviour of phenols, amines, and similar compounds in aromatic nitration as compared with that of other aromatic molecules (cf. Bunton, Hughes, Ingold, Jacobs, Jones, Minkoff, and Reed, *J.*, 1950, 2628; Blackall, Hughes, and Ingold, *J.*, 1952, 29) being borne in mind.

For these reasons the exchange behaviour of benzene was studied as a function of solvent acidity. The difficulties involved in separating a small quantity of this compound from a large amount of aqueous acid were overcome by the application of an isotope dilution technique, which also permitted low concentrations of benzene (~0·007M) to be used. Although several earlier investigations have dealt with the exchange behaviour of benzene, the present work is believed to be the first quantitative study of this reaction under homogeneous conditions.

Experimental

(a) *Preparation of Monodeuterobenzene* ([$^2H_1$]*Benzene*).—The method of preparation has been described by Bryce-Smith, Gold, and Satchell (*J.*, 1954, 2743). Isotopic analysis (method described by *idem, loc. cit.*) showed the product to contain: C_6H_5D, 89·5; C_6H_6, 10·5 mol.%.

(b) *Procedure for Kinetic Experiments.*—The rate of loss of deuterium from the prepared deuterobenzene to six different sulphuric acid–water mixtures was studied. The acids had H_0 (Hammett's acidity function) values varying from −5·08 to −7·34. For each acid accurately measured samples (~0·15 ml.) of the prepared benzene were dissolved in samples (220 ml.) of the acid contained in flasks (250 ml.) fitted with ground-glass stoppers and having an additional

* Part II, preceding paper.

sealing of Apiezon " Q compound." The flasks were kept in a thermostat at 25°, for suitable known times. On removal from the bath a flask was opened, and a measured amount (~1·3 ml.) of " AnalaR " benzene added to its contents, which, after resealing of the flask, were agitated for 15 min. Previous experiments had shown that equilibration between dissolved and added benzene was essentially complete well within such a period. The benzene and acid phases were now separated, and the benzene washed with water and stored over a little barium carbonate and calcium chloride in a sealed flask. Isotopic analysis of such samples (together with the assumption that there is no isotopic fractionation in the equilibration) allows the composition of the dissolved benzene to be determined, and hence the exchange rate to be calculated.

(c) *Method of Isotopic Analysis.*—The infrared spectrum of liquid monodeuterobenzene possesses bands at 11·6 and 12·8 μ (cf. Bailey, Gordon, Hale, Herzfeld, Ingold, and Poole, *J.*, 1946, 299), absent from the spectrum of ordinary benzene, which permit quantitative analysis of mixtures of these two compounds. On using a Grubb-Parsons S4 double-beam spectrometer with rock-salt optics and fixed rock-salt cells of ~0·003 cm. thickness, calibration with a series of mixtures of known composition showed Beer's law to be approximately obeyed (see Fig. 1). The cells were always recalibrated at the time of each series of measurements to obviate any error which might otherwise be introduced owing to deterioration of the rock-salt surfaces with time,

FIG. 1. *Cell calibration at* 12·8 μ.

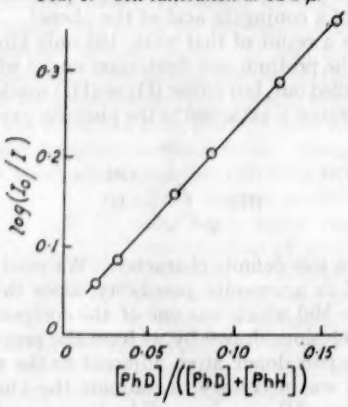
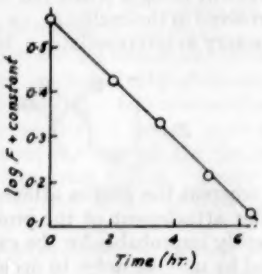


FIG. 2. *Example of first-order exchange reaction.*



etc. Trial experiments using the isotopic dilution method described above showed that it was possible to determine the isotopic composition of an unknown, dissolved sample to ±1·0 mol.% of C_6H_5D over the range 0—90 mol.%.

The proportion of deuterium in the exchanging system being very small, the kinetics would be expected to be of the first order (Harris, *Trans. Faraday Soc.*, 1951, **47**, 716; Melander, *Arkiv Kemi*, 1954, **7**, 287). A specimen first-order plot is shown in Fig. 2. The first-order rate constants, λ, are tabulated together with the corresponding H_0 values in Table 1, and plotted against them in Fig. 3, the slope of the line being 1·36.

TABLE 1. *Dependence of the exchange rate on acidity.*

H_2SO_4 (wt. %)	66·5	68·7	73·5	75·8	79·2	83·2
$-H_0$	5·08	5·40	5·99	6·27	6·72	7·34
$10^7\lambda$ (sec.$^{-1}$)	2·68	5·75	35·2	115·0	453	3450

(d) *Sulphonation.*—The method of analysis, involving as it does, isotopic dilution of the sample undergoing exchange, obviously requires that there be no loss of benzene from the reaction flasks. Any sulphonation or evaporation from the flask would mean such a loss. It was possible to estimate the extent of sulphonation by reversing the dilution procedure used for studying the exchange rate. Accurately measured samples (~0·15 ml.) of " AnalaR " benzene were dissolved in samples (220 ml.) of the strongest acid used for exchange and, after various time intervals, the solutions were equilibrated with a suitable C_6H_6–C_6H_5D mixture. Isotopic analysis of the resulting samples showed sulphonation and other losses to be slight during the period occupied by the exchange experiments involving this acid. Such a situation

was assumed to hold for the other (weaker) acids also (cf. Ingold, Raisin, and Wilson, *J.*, 1936, 915). A more detailed investigation of the rates of sulphonation is now in progress.

Discussion

The dependence of reaction velocity upon acidity is shown in Fig. 3, and is of the same general form as for the substituted phenols (Part II, *loc. cit.*). There is a quantitative difference between the slopes found for the different aromatic compounds but it is thought that this is a secondary effect (see Part IV, following paper) and that it does not point to any abnormal behaviour of benzene compared with that of the substituted phenols. It is therefore concluded that the mechanism of hydrogen isotope exchange is the same in all these cases.

This view is reinforced by the actual magnitudes of the rates of exchange for the various compounds. For the exchange reaction we have found that benzene and *p*-nitrophenol are about equally reactive. It has been shown that at high concentrations of nitric acid (10M) in glacial acetic acid and low concentrations of nitrous acid the mechanisms of nitration of these two compounds are identical and involve attack by the NO_2^+ ion. A rough comparison of the velocities is possible from the rate constants given by Bunton *et al.* (*loc. cit.*, Table X) and by Hughes, Ingold, and Reed (*J.*, 1950, 2400, Table IV). Such a comparison reveals approximately the same relative reactivity (per nuclear position) as we have found for exchange.

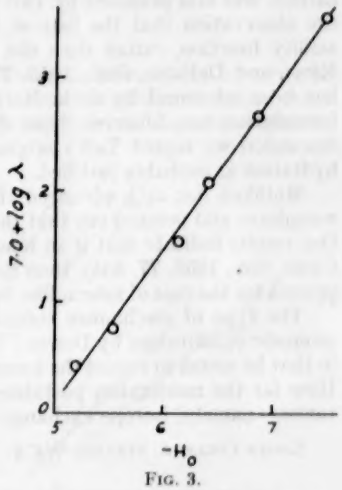
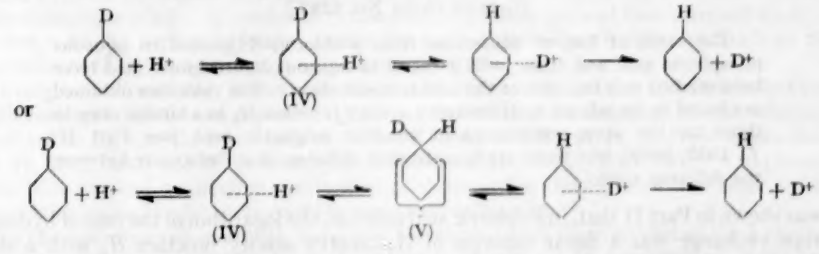


Fig. 3.

Dependence of exchange rate on acidity.

The mechanism for benzene being the same as that for the substituted phenols, it follows that a conjugate acid of benzene of a type which we formulate non-commitally as (IV), must be involved as an intermediate in the exchange reaction of benzene. By analogy, the result also indicates that (III) is more likely than (II) to be the formula for the intermediate in the case of the exchange reaction with phenols. The complete mechanism for benzene is (cf. Part II, *loc. cit.*) illustrated in the annexed scheme. The existence of (V) [analogous to (I)] as a stable intermediate is not essential to the kinetics, but the possible scheme involving it is presented in order to show how the exchange mechanism is related to those of the other electrophilic aromatic substitution reactions, such as nitration, which are widely thought to involve similar intermediates, and because there is some other evidence that such structures do exist (see below).



The formulation of (III) and (IV) clearly requires some non-classical concept of chemical interaction. It seems convenient to apply to the structures (I), (III), (IV), and (V) the terminology proposed by Mulliken (*J. Phys. Chem.*, 1952, **56**, 801, 821), referring to (I) and (V), where the entering and leaving substituents occupy equivalent positions, as

" inner complexes " and to (III) and (IV) as " outer complexes." Structures of this type have also been considered by Brown and Brady (*J. Amer. Chem. Soc.*, 1952, **74**, 3570) who termed them σ- and π-complexes respectively but, in view of the different interpretations placed on the term " π-complex " by different authors (cf. *idem*, *ibid.*), it seems preferable to avoid the name.

Two other investigations dealing with the interaction between acids and aromatic or unsaturated systems have led to conclusions very similar to those outlined in the present paper. Brown and Brady (*loc. cit.*), investigating the equilibria between hydrochloric acid and aromatic hydrocarbons, with and without added aluminium trichloride, suggested that the conjugate acid of benzene formed in the first case was an inner complex and in the second an outer complex. Only the interaction which leads to an inner complex can result in hydrogen isotope exchange between deuterium chloride and benzene (Klit and Langseth, *Z. phys. Chem.*, 1936, **176**, 65). Again, a mechanism essentially identical with ours, involving the slow interconversion of two distinct conjugate acids of the same hydrocarbon, was first proposed by Taft (*J. Amer. Chem. Soc.*, 1952, **74**, 5372) in order to explain the observation that the rate of hydration of *iso*butene appeared to follow Hammett's acidity function, rather than the concentration of hydrogen ions (see also Taft, Purlee, Riesz, and DeFazio, *ibid.*, 1955, **77**, 1584). A more general formulation of Taft's results has been advanced by de la Mare, Hughes, Ingold, and Pocker (*J.*, 1954, 2930). This formulation has, however, been discussed in Part II (*loc. cit.*), and in the light of that discussion we regard Taft's original specific representation of the mechanism of olefinic hydration as probably justified.

Mulliken (*loc. cit.*) advanced theoretical reasons for the existence of inner and outer complexes and pointed out that there may or may not be an energy barrier between them. Our results indicate that if an inner complex is, in fact, involved (cf. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334), then the transition from an outer complex to it *is* an activated process for the case of interaction between a proton and an aromatic structure.

The type of mechanism considered in this paper is different from that suggested for aromatic substitution by Dewar (" Electronic Theory of Organic Chemistry," Oxford, 1949) in that he seems to regard the formation of an outer or π-complex as the probable slow step. How far the mechanism postulated by us for the simplest electrophilic aromatic substitution—namely, isotope exchange—is applicable in other cases is, at present, speculation.

KING'S COLLEGE, STRAND, W.C.2. [*Received, April 27th*, 1955.]

The Kinetics of Hydrogen Isotope Exchange Reactions. Part IV. A Comparison of the Exchange Reactivity of Different Aqueous Acids.*

By V. GOLD and D. P. N. SATCHELL.

[Reprint Order No. 6362.]

The rates of loss of deuterium from *p*-chloro[*o*-^{2}H]phenol in aqueous phosphoric acid and from [*o*-^{2}H]*p*-cresol in aqueous hydrochloric acid have been studied as a function of the acid concentration. The velocities obtained are found to be related to Hammett's acidity function H_0 in a similar way to those for the same compounds in aqueous sulphuric acid (see Part II, *J.*, 1955, 3609), but there are quantitative differences in behaviour between the different acids.

IT was shown in Part II that, in sulphuric acid solution, the logarithm of the rate of hydrogen isotope exchange was a linear function of Hammett's acidity function H_0 with a slope close to the theoretical value of −1. If this correlation is, in fact, significant and not just fortuitous in the particular case of sulphuric acid, then the same relation should be obeyed when other acids are used. This point has been tested in the present investigation.

* Part III, preceding paper.

Experimental.—The reagents and experimental methods used were the same as those described in Part II (*loc. cit.*). The results are tabulated below.

Rate of loss of deuterium from [*o*-^{2}H] p-*cresol in aqueous hydrochloric acid.*

HCl (wt. %)	7·10	11·66	15·16	21·55
$-H_0$ [1]	0·58	0·98	1·31	1·90
$10^7\lambda$ (sec.$^{-1}$) [2]	3·95	13·3	38·9	306·0

[1] Taken from Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 828. [2] Defined by equation (1), Part II (*loc. cit.*).

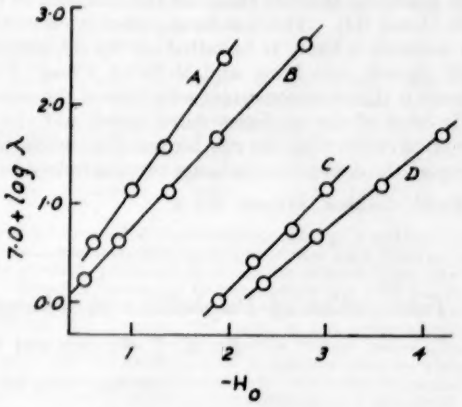
Rate of loss of deuterium from p-*chloro*[*o*-^{2}H]*phenol in aqueous phosphoric acid.*

H_3PO_4 (wt. %)	63·6	68·1	72·7	76·4
$-H_0$ [1]	1·90 ± 0·1	2·25 ± 0·1	2·65 ± 0·1	3·00 ± 0·1
$10^7\lambda$ (sec.$^{-1}$) [2]	1·17	2·67	5·6	14·8

[1] Taken from Heilbronner and Weber, *Helv. Chim. Acta*, 1949, **32**, 1513. [2] Defined by equation (1), Part II.

Discussion

The results of this investigation follow the same general pattern as those reported in Part II, in that the rates are again found to depend on Hammett's acidity function, log λ being linearly related to $-H_0$. For *p*-chlorophenol in phosphoric acid and in sulphuric



Dependence of exchange rate on acidity.
A, p-*Cresol in* HCl.
B, p-*Cresol in* H_2SO_4.
C, p-*Chlorophenol in* H_3PO_4.
D, p-*Chlorophenol in* H_2SO_4.

acid, the respective slopes of the graphs are 1·00 and 0·90. For *p*-cresol in hydrochloric acid the slope is 1·42, and in sulphuric acid it is 1·08. From the Figure it can be seen that, because of these differences in slope, the rate constants referring to different acids diverge with increasing acidity. If produced to lower acidities both pairs of lines intersect at H_0 = 0·5—0·0. At the highest acidities, values for log λ obtained with different acids at the same value of H_0 differ by as much as 0·4 unit.

Divergences from the theoretical slope and differences in the detailed behaviour of different acids have been reported before in connection with reactions whose velocities are related to H_0, *e.g.*, the hydrolysis of methylal (Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3240, 3243) and of acetic anhydride (Gold and Hilton, *J.*, 1955, 843). The present results bear marked qualitative similarities to these earlier data (which also refer to the same acidity region) and may be usefully compared with them.

For the hydrolysis of methylal, Long and McIntyre found that the plot of log k against $-H_0$ showed a slope of ~1·25 for hydrochloric acid and ~1·15 for sulphuric acid, and their rates, like ours, are equal at H_0 ~0·5 but diverge towards high acidities, those in hydrochloric acid being the faster. These authors have given a semiquantitative explanation of the different divergences from unit slope in the various acids in terms of specific salt effects. On this basis, since the deuterium exchange involves a different substrate

from the hydrolysis, an exact agreement between the two reactions is hardly to be expected, as this would imply a fortuitous identity of the salt effects in the two cases. However, the observed parallelism indicates a similar behaviour of the relevant activity coefficients in the two acids.

The data on the hydrolysis of acetic anhydride refer to sulphuric acid, hydrochloric acid, and phosphoric acid so that a more complete comparison with our exchange data is possible. Gold and Hilton found that for these three acids the slopes of the log k against $-H_0$ plots were 0·96, 1·33, and 0·86 respectively. For both reactions the hydrochloric acid and phosphoric acid plots lie above that for sulphuric acid. Here again therefore the results show a similar trend and the departures from ideal behaviour in the two cases probably have similar origins.

The rather steep slopes recorded above for the reactions in hydrochloric acid may be partly due (and this suggestion is made with considerable diffidence) to slight inaccuracies in the (rather old) H_0 data (Hammett and Paul, *J. Amer. Chem. Soc.*, **1934**, **56**, 828) used in plotting the graphs in all three investigations. If data taken from more recent but less extensive measurements (Braude, *J.*, **1948**, 1971; Paul, *J. Amer. Chem. Soc.*, **1954**, **76**, 3236) are used, the slopes of the plots are considerably reduced, though not sufficiently to bring them exactly to unity. The three available sources of hydrochloric acid acidity function data disagree above 1M.

For the benzene–sulphuric acid exchange the slope of the log λ–H_0 plot differs from -1 more markedly than do those for the reactions of the substituted phenols in this acid (see Parts II and III). This is to be expected in view of Long and McIntyre's explanation, since this molecule is likely to be salted out by sulphuric acid more strongly than are the substituted phenols (see Long and McDevit, *Chem. Rev.*, 1952, **51**, 119). The behaviour of benzene is therefore consistent with that of the other compounds.

In view of the analogies noted above and the fact that a slope of exactly -1 is the exception rather than the rule for reactions whose rates are related to H_0, it seems legitimate to regard the deuterium exchange rates as indeed being so related.

King's College, Strand, W.C.2. [*Received, April 27th*, 1955.]

Intervention of Polyhalides in Thionyl Bromide–Alcohol Systems.

By M. J. Frazer and W. Gerrard.

[Reprint Order No. 6469.]

Thionyl bromide and pyridinium bromide readily form pyridinium tribromide which functions as bromine and pyridinium bromide, whereas pyridinium trichloride has not been obtained from corresponding reagents. Therefore, in thionyl bromide–alcohol–pyridine systems complications arise which have not been discerned in thionyl chloride ones. Intervention of tribromide ion leads to reduced yields and rotatory power of alkyl bromide, and to halogenation of a double bond in the alcohol. These complications are largely avoided by using thionyl bromide, a trace of pyridinium bromide, and previously formed sulphite. Experiments with other trihalide ions are described.

Interaction of thionyl chloride and an alcohol of ordinary reactivity (such as *n*-butanol) includes the sequence of reactions (1)—(4) (see Gerrard, Machell, and Tolcher, *Research*, 1955, **8**, S7; Gerrard and Schild, *Chem. and Ind.*, 1954, 1232). In the presence of pyridine, the base hydrochloride formed during reactions (1) and (2) powerfully accelerates (3) and rather less effectively (4). Intervention by pyridinium trichloride, $C_5H_5NHCl_3$, has not been discerned; for, although there is evidence that the trichloride can exist, it is probably not formed by the interaction of thionyl chloride and pyridinium chloride (Frazer and Gerrard, *Research*, 1954, **7**, S27). On the other hand, pyridinium tribromide is readily

formed during the addition of thionyl bromide to base hydrobromide, and its intervention weakens the analogy between the thionyl bromide and the thionyl chloride system.

$$BuOH + SOCl_2 \xrightarrow{quick} BuO{\cdot}SOCl + HCl \quad . . . . . (1)$$

$$BuOH + BuO{\cdot}SOCl \xrightarrow{quick} (BuO)_2SO + HCl \quad . . . . . (2)$$

$$(BuO)_2SO + SOCl_2 \xrightarrow{slow} 2BuO{\cdot}SOCl \quad . . . . . (3)$$

$$BuO{\cdot}SOCl \xrightarrow{slow} BuCl + SO_2 \quad . . . . . (4)$$

Other trihalides, *e.g.*, Cl_2Br^-, Br_2Cl^-, Cl_2I^-, Br_2I^-, are obtained from pyridinium halide and the appropriate thionyl halide (5), and in Table 2 are recorded results of the interaction

$$2SOX_2 + 2C_5H_5NHY \longrightarrow 2C_5H_5NHX_2Y + S + SO_2 \quad . . . . . (5)$$

of these trihalides with di-*n*-butyl sulphite. Trihalides can function as a monohalide and halogen or interhalogen compound, the smaller halogen remaining as the base hydrohalide. Thus the trihalide $C_5H_5NHClBr_2$ functions as bromine and the hydrochloride, and

TABLE 1.

Pyridinium polyhalide	Method †	Yield (%)	M. p.	Colour	Halogen (equiv./mole): total	Halogen (equiv./mole): available	Found (%): C	Found (%): H	Calc. (%): C	Calc. (%): H
Cl_2 *	*a*	91	50—55°	Light yellow	2·45	1·56	—	—	—	—
$BrCl_2$	*b*	93	136—137	Yellow	2·92	1·97	27·1	2·6	26·0	2·6
Br_2Cl * ...	*c*	59	94—96	Orange	3·00	1·99	23·7	2·4	21·8	2·2
Br_3	*c*	75	135	Red	2·95	1·89	24·0	1·8	24·7	1·9
Cl_2I	*d*	78	187	Yellow	2·72	2·03	21·9	2·5	21·6	2·2
Br_2I	*d*	84	176—177	Brown	2·91	1·91	16·7	1·8	16·4	1·65
ClI_2 *	*e*	68	65—70	Black	2·92 *f*	2·14	17·1	1·9	16·2	1·6
BrI_2 * ...	*e*	64	139—141	Black	2·82 *f*	1·86	15·2	1·0	14·5	1·5

* New compounds.

† (*a*) Liquid chlorine (26·0 g., 2 mol.) was added to pyridine hydrochloride (22·0 g., 1 mol.) at −80° During 0·5 hr. at 20° chlorine (16·0 g., 1·2 mol.) was lost, leaving a light yellow solid (32·0 g.), but there was no further loss in weight when the product, protected by a calcium chloride tube, was left open to the atmosphere for 18 hr. at 20°. However, attempts to recrystallise the solid led to its decomposition, and loss of chlorine. (*b*) Chlorine was passed through a suspension of pyridine hydrobromide in carbon tetrachloride and chloroform. (*c*) Bromine was added to the hydrochloride or hydrobromide. (*d*) These compounds were prepared from the appropriate thionyl halide (Frazer and Gerrard, *Research*, 1954, **7**, S27). (*e*) Iodine and the hydrochloride or hydrobromide were mixed in glacial acetic acid. (*f*) To obtain these figures it was found necessary to reduce the compound as follows. Sulphur dioxide was passed (5 min.) through a warm alcoholic solution of a sample of the compound, and total halogen was then determined by a Volhard titration.

$C_5H_5NHCl_2Br$ as bromine chloride and hydrochloride. If we assume analogy with chlorine (Levaillant, *Ann. Chim.*, 1936, **6**, 461; Gerrard, *J.*, 1940, 218; Cross and Gerrard, *J.*, 1949, 2686) bromine should react according to (6), and bromine chloride to (7).

$$(BuO)_2\overset{\overset{O}{\|}}{S}: \dashrightarrow Br{-}Br \quad Br^- \dashrightarrow \left[BuO{-}\overset{\overset{Br}{|}}{\underset{\underset{O}{\|}}{S}}{-}OBu\right]^+ \quad . . . . . (6)$$

$$\longrightarrow BuBr + BuO{\cdot}SO_2Br$$

$$(BuO)_2\overset{\overset{O}{\|}}{S}: \dashrightarrow Br{-}Cl \quad Cl^- \dashrightarrow \left[BuO{-}\overset{\overset{Br}{|}}{\underset{\underset{O}{\|}}{S}}{-}OBu\right]^+ \quad . . . . . (7)$$

$$\longrightarrow BuCl + BuO{\cdot}SO_2Br$$

In the example of the dibromochloride, alkyl chloride can still be formed, because chloride ions from the base hydrochloride can compete with bromide ions during the second stage of the sequence of reactions. From the nature of chlorosulphonates (see Levaillant; and Cross and Gerrard, *locc. cit.*), it may be expected that bromosulphonates will tend to

give alkyl bromide and consequently a mixture of alkyl halides results when the dichlorobromide is used. It is noticeable that trihalides containing iodine react much more slowly, and although this may be partly due to their known stability in dissociating conditions, it is probable that iodine halide reacts much more slowly with the sulphite.

TABLE 2.

Pyridinium polyhalide	g.	$(RO)_2SO$ g. (1 mol.)	Time (hr.)	Temp.	Method	Alkyl halide g.	Alkyl halide b. p.	Alkyl halide n_D^{20}	Alkyl halide d_4^{20}	RCl (mol.)	RBr (mol.)	2nd Fraction (g.)	Solid residue (g.)
Cl_2	12·70	13·00	50	20°	*A*	7·30	78—79°	1·4022	0·892	1·1	—	—	12·3
$BrCl_2$	11·40	9·70	143	20	*B*	7·70	78—90	1·4100	0·971	1·25	0·28	0·8	8·9
Br_2Cl	13·70	9·70	265	20	*B*	6·40	78—98	1·4230	—	0·67	0·73	0·7	14·6
Br_3Cl	13·70	19·40 (2 mol.)	7	70	*B*	12·55	78—100	1·4280	—	0·68	1·38	5·5 [a]	11·25
Br_2	8·00	4·95	120	20	*A*	4·35	99—100	1·4400	1·270 [b]	—	1·3	—	7·75 [c]
Cl_2I	3·20	2·20	6	70	*C*	—	—	—	—	—	—	2·1 [d] 96%	3·20 [e]
Br_2I	16·45	8·75	6	70	*C*	0·20	100	—	—	—	—	7·45 [f] 86%	15·50 [g]
ClI_3	15·70	8·30	6	70	*C*	0·30	—	—	—	—	—	6·20 [h] 75%	13·80 [i]

(*a*) On distillation gave some dibutyl sulphate (2·3 g.), b. p. 56—74°/0·4 mm., n_D^{18} 1·4315, which can be obtained by the interaction of alkyl sulphite and alkyl chlorosulphonate (see Levaillant, *Compt. rend.*, 1933, **197**, 648). (*b*) Found: Br, 57·6. Calc. for C_4H_9Br: Br, 58·3%. (*c*) After recrystallisation from glacial acetic acid, pyridine hydrobromide (3·75 g., 0·95 mol.), m. p. 210—213° (Found: Br, 49·6. Calc. for C_5H_5NBr: Br, 50·0%), was obtained. (*d*) Di-*n*-butyl sulphite, b. p. 104°/12 mm., n_D^{20} 1·4280. (*e*) M. p. 187° (Found: equiv. of available halogen/mole, 1·91). (*f*) Di-*n*-butyl sulphite, b. p. 102°/8 mm., n_D^{19} 1·4280. (*g*) M. p. 173° (Found: equiv. of available halogen/mole, 1·91). (*h*) Di-*n*-butyl sulphite, b. p. 110°/20 mm. (*i*) Found: equiv. of available halogen/mole, 1·97.

TABLE 3.

Alcohol	$(RO)_2SO$ (g.)	C_5H_5NHBr (g.) *	Alkyl bromide Yield (%)	Alkyl bromide B. p.	Alkyl bromide n_D^{20}	Br (%) Found	Br (%) Calc.
Butan-2-ol	4·70	(i) 0·02	75	92°	1·4380	57·9	58·4
		(ii) 4·00	63	92	1·4380	58·2	
Allyl alcohol	3·70	(i) 0·05	61	70	1·4673	65·7	66·05
		(ii) 4·00	6	70	1·4620	—	—
But-1-en-3-ol	3·83 [a]	(i) 0·03	74	98—102	1·4750	57·6	59·2
		(ii) 6·40	48	100—104	1·4740	58·1	
Hex-1-en-3-ol	4·92 [b]	(i) 0·02	56	68—70/45 mm.	1·4680	47·6	49·0 †
		(ii) 6·40	21	70/50 mm.	1·4633	47·1	
2-Methylpent-2-en-4-ol	4·92 [c]	(i) 0·02	40	80—90/10 mm.	1·4995	46·8	49·0 †
		(ii) 6·40	14	80—90/10 mm.	1·4993	—	
2-Methylpent-1-en-4-ol	4·92 [d]	(i) 0·02	34	66—70/7 mm.	1·4990	44·6	49·0 †
		(ii) 6·40	21	66—70/7 mm.	1·4990	45·7	

* (i) 0·01 Mol.; (ii) 2 mol.

† Available material was too small for further purification to be practicable.

(*a*) B. p. 98°/20 mm., n_D^{20} 1·4463 (Found: S, 16·7. $C_8H_{14}O_3S$ requires S, 16·9%). (*b*) B. p. 98—100°/0·1 mm., n_D^{20} 1·4630 (Found: S, 13·3. $C_{12}H_{22}O_3S$ requires S, 13·0%). (*c*) B. p. 98°/1·0 mm., n_D^{20} 1·4561 (Found: S, 12·5. $C_{12}H_{22}O_3S$ requires S, 13·0%). (*d*) B. p. 90—93°/1·0 mm., n_D^{20} 1·4570 (Found: S, 12·8. $C_{12}H_{22}O_3S$ requires S, 13·0%).

In Table 3 are shown the marked differences in the yields of alkyl bromide formed when thionyl bromide is added to the sulphite of an unsaturated alcohol in the presence of either 0·01 mol. or 2 mols. of pyridine hydrobromide. The pyridinium tribromide present in quantity can be used up in brominating the double bond, whereas when only a small amount of tribromide is present, the main reactions correspond to (3) and (4) catalysed by the salt, either bromide or tribromide.

When correlating mechanisms with the rotatory power of the alkyl halide produced, it is essential to know the nature of every reaction contributing to the overall yield of that product. In Table 4 are recorded the yields and optical rotations of the specimens of

2-bromo-octane obtained under different conditions in the thionyl bromide system. It is clear that the highest yield and greatest retention of optical activity (inversion of configuration) occur when thionyl bromide is added to the sulphite in the presence of a *trace* of pyridine hydrobromide (see Frazer, Gerrard, Machell, and Shepherd, *Chem. and Ind.*, 1954, 931).

TABLE 4.

Reactants	ROH α_D^{20} ($l = 1$)	Yield (%) [a]	B. p./mm.	n_D^{20}	d_4^{20}	Br (%) [b]	α_D^{20} ($l = 1$)	% Retention of optical activity (inversion) [c]
$(RO)_2SO + SOBr_2 +$ C_5H_5NBr (0·01 mol.)	−7·64°	71·3	72°/10	1·4495	1·093	40·6	+36·72°	87
$(RO)_2SO + SOBr_2$ alone [d]	−7·60	57·6	76/12	1·4500	—	41·4	+36·00	86
$2ROH + 2SOBr_2 +$ $2C_5H_5N$ (2 mol.)	−7·64	51·3	72/10	1·4500	1·093	41·9	+35·80	85
$(RO)_2SO + SOBr_2 +$ C_5H_6NBr (2 mol.) ...	−7·64	53·8	72/10	1·4492	—	41·05	+35·20	84
$2ROH + 2SOBr_2$	−7·64	50·6	72/10	1·4497	1·098	40·9	+34·32	82
$(RO)_2SO + C_5H_5NHBr_3$	−7·60	45·0	82/15	1·4505	1·101	41·2	+28·72	68·5
$(RO)_2SO + C_5H_5NHBr_3$ [e]	−6·62	45·0	74—76/11	1·4500	1·097	41·7	+23·12	64
$(RO)_2SO + Br_2$ [f]	−7·60	29·8	78/12	1·4522	—	41·9	+24·00	57

(*a*) The yields in all cases are based on an expectation of 2 mol. of the bromide. (*b*) Calc. for $C_8H_{17}Br$: Br, 41·4%. (*c*) Calculated on the assumption that the (−)-ROH (α_D^{20} −8·00°) gives the (+)-RBr (α_D^{20} +44·00°) (Gerrard, *J.*, 1945, 848). (*d*) At 60° for 3 hr. (*e*) At 20° for 192 hr. (*f*) At 70° for 1·5 hr.

EXPERIMENTAL

Formation of Pyridinium Polyhalides.—Although the polyhalides were made from the base hydrohalide and thionyl halide by Frazer and Gerrard (*loc. cit.*), for the present purpose some of these were prepared by the addition of halogen to the monohalide, and were recrystallised from glacial acetic acid. Details are shown in Table 1. Analyses were carried out as described by Frazer and Gerrard (*loc. cit.*). Thionyl bromide was prepared by their method (*Chem. and Ind.*, 1954, 280).

*Interaction of Pyridinium Polyhalides and Di-*n*-butyl Sulphite.*—The results are shown in Table 2. For polyhalides containing iodine the amount of dibutyl sulphite recovered is shown in the column headed "2nd Fraction." In the other cases, sulphur dioxide was evolved, and the colour of the polyhalide faded.

The methods of isolating the alkyl halide were as follows: (*A*) The halide was removed from the reaction mixture at 20°/10 mm. (1 hr.) and collected at −80°. (*B*) The supernatant liquid was decanted off, and process (*A*) used to complete removal from residue. The liquids were combined. (*C*) The mixture was filtered and washed with anhydrous ether (50 c.c.), the ether removed from the filtrate, and the residue dried at 10 mm.

The composition of the reaction product (1-chloro- and 1-bromo-butane) was estimated from the refractive index of the mixture, a graph constructed from the refractive indices of mixtures of known composition being used.

Interaction of Thionyl Bromide and the Sulphites of a Number of Unsaturated Alcohols in the Presence of Pyridine Hydrobromide (i, 0·01 *Mol.*; ii, 2 *Mols.*).—The results are shown in Table 3. Thionyl chloride (0·5 mol.) in anhydrous ether (25 c.c.) was added slowly (0·25—0·5 hr.) to a mixture of pyridine (1 mol.) and the alcohol (1 mol.) in ether (25 c.c.) at −80°. The pyridine hydrochloride was filtered off, the ether removed at 10 mm., and the sulphite distilled. To the sulphite (1 mol.), at −80°, were added pyridine hydrobromide (i, 0·01 mol.; ii, 2 mols.) and thionyl bromide (1 mol.). The mixture was allowed to warm to 20° (10 min.) and then heated to 70° for 3 hr., whereupon there was a vigorous evolution of sulphur dioxide. The reaction mixture was added to water (10 c.c.) and the oily layer was separated and distilled. A higher-boiling fraction was also obtained, leaving a black solid residue.

Interaction of Thionyl Bromide (1 *Mol.*) *with Pyridine* (1 *Mol.*) *and Allyl Alcohol* (1 *Mol.*).—Thionyl bromide (20·80 g., 1 mol.) was added (0·75 hr.) to a mixture of allyl alcohol (5·80 g., 1 mol.) and pyridine (7·90 g., 1 mol.) at −10°. The mixture was heated at 100° for 3 hr., whereupon sulphur dioxide was evolved and the precipitate dissolved. On cooling, a yellow solid formed which was added to water (50 c.c.) and extracted with ether (50 c.c.). The ethereal solution was dried ($MgSO_4$) and distilled, giving a mixture of ether and allyl bromide, b. p. 39—45°, and then 1 : 2 : 3-tribromopropane (7·2 g., 0·25 mol.), b. p. 92°/8 mm., n_D^{20} 1·5710, d_4^{20} 2·259.

Bromine was added to the first fraction until it was slightly red, the ether was removed at 10 mm., and the residue gave 1 : 2 : 3-tribromopropane (9·8 g., corresponding to allyl bromide, 35%), b. p. 103°/15 mm., n_D^{20} 1·5713.

Interaction of Pyridinium Tribromide and Allyl Alcohol.—Allyl alcohol (2·9 g., 1 mol.) was added quickly to pyridinium tribromide (16·00 g., 1 mol.). The solid was immediately decolorised with evolution of heat. The reaction mixture was added to water (20 c.c.) and extracted with ether (20 c.c.). The ethereal solution was dried ($MgSO_4$) and after removal of ether gave 2 : 3-dibromopropan-1-ol (7·1 g., 66%), b. p. 100°/8 mm., n_D^{18} 1·5600, d_4^{20} 2·122 (Found : C, 17·0; H, 2·7. Calc. for $C_3H_6OBr_2$: C, 16·5; H, 2·8%). The aqueous washings contained 3·9 g. of bromine (Calc. for 1 mol. of C_3H_6NBr : 4·0 g.).

Formation of (+)-2-Bromo-octane.—The reactants shown in Table 4 were heated at 70° for 3 hr. and then the reaction mixture was dissolved in water (15 c.c.), extracted with ether (20 c.c.), dried ($MgSO_4$), and the ether removed. After initial distillation of the (+)-2-bromo-octane, traces of alcohol were removed by means of thionyl chloride and pyridine, before final distillation.

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A Novel Method of Cyanoethylation. Part III. The Mechanism of the Reaction.*

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Reaction of 2-diethylaminoethyl cyanide with arylamine salts to give *N*-2-cyanoethylarylamines is shown to proceed by a substitution mechanism, rather than by elimination followed by addition. The use of *N*-deutero-diethylamine confirms this conclusion.

In Part I (*J.*, 1951, 3311) the reaction of 2-diethylaminoethyl cyanide with arylamine salts at 180° was shown to lead to *N*-2-cyanoethylarylamines. This amine-exchange cyanoethylation may proceed either by elimination (reaction 1) followed by Michael addition (reaction 2), or alternatively by a substitution mechanism (reaction 3) followed by proton transfer to the more strongly basic dialkylamine (reaction 4).

After Part I had been submitted, a paper by Bekhli came to hand [*J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 86] in which he prepared *N*-2-cyanoethylarylamines from 2-cyanoethyldiethylammonium chloride and arylamines at 140—160° (2 hr.). He states that the reaction proceeds by cleavage followed by addition, *i.e.*, reactions 1 and 2, and cites as evidence his finding that, whereas 2-diethylaminoethyl cyanide remained substantially unchanged at 193° for 3 hr., its hydrochloride when heated alone to 160—190° gave 77% of vinyl cyanide. The dissociation of Mannich bases, on distillation, into

$$CN\cdot CH_2\cdot CH_2\cdot \overset{+}{N}HEt_2\}\bar{X} \rightleftharpoons CN\cdot CH{:}CH_2 + \overset{+}{N}H_2Et_2\}\bar{X} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CN\cdot CH{:}CH_2 + NH_2Ar \longrightarrow CN\cdot CH_2\cdot CH_2\cdot NHAr \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CN\cdot CH_2\cdot CH_2\cdot \overset{+}{N}HEt_2\}\bar{X} + NH_2Ar \longrightarrow CN\cdot CH_2\cdot CH_2\cdot \overset{+}{N}H_2Ar\}\bar{X} + NHEt_2 \quad . \quad . \quad (3)$$

$$CN\cdot CH_2\cdot CH_2\cdot \overset{+}{N}H_2Ar\}\bar{X} + NHEt_2 \longrightarrow CN\cdot CH_2\cdot CH_2\cdot NHAr + \overset{+}{N}H_2Et_2\}\bar{X} \quad . \quad . \quad (4)$$

the amine and an ethylene is well known, and it is expected that salt formation will enhance the rate of such elimination, which presumably proceeds by the "*E1cB*" mechanism (Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 695) or, in a medium of low dielectric constant, by an equivalent synchronous step avoiding the separation of free ions.

However, reference to Bekhli's paper showed that under his conditions (continuous removal of vinyl cyanide from a distilling flask) the elimination reaction would be expected

* Part II, *J.*, 1954, 1153.

to go towards completion, and that his findings are therefore inadmissible as proof of the "cleavage and addition" mechanism. Indeed, our own results contradict Bekhli's conclusions in this respect: we find that 2-cyanoethyldiethylammonium chloride was recovered substantially (73%) unchanged after being refluxed at 180° for 1·5 hr., thus affording evidence of the stability of this compound in the conditions used for cyanoethylation.

Further, Bekhli (*loc. cit.*) showed that no product was obtained from anilinium chloride and 2-cyanoethyldiethylammonium chloride and ascribes the formation of *N*-2-cyanoethylarylamines to reaction 2. We find, however, that no reaction occurs between vinyl cyanide and aniline, or between this cyanide and *p*-anisidinium chloride, at 180° during 1·5 hr., whereas in the same conditions 2-diethylaminoethyl cyanide and *p*-anisidinium chloride gave 78% of *N*-2-cyanoethyl-*p*-anisidine. Moreover, a mixture, in the same proportions, of vinyl cyanide, diethylamine, and *p*-anisidinium chloride afforded the same product in 67% (1·5 hr.) and 76% (2·5 hr.) yield, and reaction of vinyl cyanide, diethylammonium chloride, and *p*-anisidine gave 79% of the same substance, accompanied by some of the *NN*-di-(2-cyanoethyl) compound.

Although vinyl cyanide failed to react with either aniline or *p*-anisidinium chloride, addition of 0·1 mol. of diethylammonium benzenesulphonate to a mixture of vinyl cyanide and *p*-anisidine (1 mol. of each) led to *N*-2-cyanoethyl-*p*-anisidine in 59% yield. These results (see Table) support the hypothesis that the reaction proceeds by a substitution mechanism (reaction 3).

Reactants	Temp. (time, hr.)	Product	Yield (%)
Vinyl cyanide, diethylamine	Reflux (0·5)	2-Diethylaminoethyl cyanide	93 [4]
2-Cyanoethyldiethylammonium chloride	180° (1·5)	2-Cyanoethyldiethylammonium chloride	73
Vinyl cyanide, aniline	180 (1·5)	Unchanged	—
Vinyl cyanide, *p*-anisidinium chloride	180 (1·5)	,,	—
2-Diethylaminoethyl cyanide, aniline	180 (1)	,,	— [1]
2-Cyanoethyldiethylammonium chloride, anilinium chloride	140—150 (2)	None obtained	— [2]
2-Diethylaminoethyl cyanide, *p*-anisidinium chloride	180 (1·5)	*N*-2-Cyanoethyl-*p*-anisidine	78
Vinyl cyanide, diethylamine, *p*-anisidinium chloride	180 (1·5)	,,	68
	180 (2·5)	,,	76
Vinyl cyanide, diethylammonium chloride, *p*-anisidine	180 (1·5)	,,	79 [3]
Vinyl cyanide, *p*-anisidine, 0·1 mol. of diethylammonium benzenesulphonate	180 (1·5)	,,	59

[1] *J.*, 1951, 3311. [2] Bekhli, *loc. cit.* [3] Also isolated: *NN*-di-(2-cyanoethyl)-*p*-anisidine (7%). [4] Whitmore, Mosher, Adams, Taylor, Chapin, Weisel, and Yanko, *J. Amer. Chem. Soc.*, 1944, **66**, 725.

Further evidence has been obtained by the use of *N*-deuterodiethylamine, prepared from diethylaminomagnesium bromide and deuterium oxide and shown by mass-spectrometric analysis to contain at least 80% of $NDEt_2$; its infrared spectrum showed absorption at 2434 cm.$^{-1}$ attributable to the stretching vibration of the N–D bond (cf. deuterohydrazoic acid, 2457 cm.$^{-1}$; Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949). This band was absent from the spectrum of diethylamine, which showed only the band at 3284 cm.$^{-1}$ due to N–H.

N-Deuterodiethylamine was condensed with vinyl cyanide, the resulting 1-deutero-2-diethylaminoethyl cyanide containing, by mass-spectrometric analysis, about 80% of the deutero-compound whose infrared spectrum showed a strong band at 2244 cm.$^{-1}$ (C≡N; cf. 2252 cm.$^{-1}$ in 2-hydroxyethyl cyanide; Randall *et al.*, *op. cit.*) and a band at 2192 cm.$^{-1}$ attributable to the C–D stretching vibration (cf. 2151 cm.$^{-1}$ in 2-deuteropropane; Condon, McMurry, and Thornton, *J. Chem. Phys.*, 1951, **19**, 1010). The former, but not the latter, band was present in 2-diethylaminoethyl cyanide.

Reaction of 1-deutero-2-diethylaminoethyl cyanide and *p*-anisidinium benzenesulphonate gave diethylammonium benzenesulphonate which, on treatment with saturated

sodium hydroxide solution, evolved diethylamine containing no $NDEt_2$: the mass-spectrometer would have detected 2% of this substance.

The absence of deuterium in the diethylammonium benzenesulphonate shows that the CH_2·CHD·CN group remained intact during the reaction and hence provides further evidence for a nucleophilic substitution mechanism. The *N*-2-cyanoethyl-*p*-anisidine was not volatile enough to give a reading in the ion chamber of the mass-spectrometer, but its infrared spectrum showed both a strong band at 2243 cm.$^{-1}$ (C≡N) and a very weak peak at 2192 cm.$^{-1}$ (C–D) corresponding exactly in wavelength with that found in 1-deutero-2-diethylaminoethyl cyanide.

Experimental

Stability of 2-Cyanoethyldiethylammonium Chloride.—2-Cyanoethyldiethylammonium chloride [32·5 g., 0·2 mole; Terent'ev and Kost, *J. Gen. Chem.* (*U.S.S.R.*), **1946**, **16**, 859] was heated under reflux for 1·5 hr. at 180°. The cooled material was thoroughly washed (dry C_6H_6), and the residue basified with sodium hydroxide solution (pH >12) and extracted with ether. Removal of solvent from the dried (Na_2SO_4) extracts on the steam-bath gave 2-diethylaminoethyl cyanide (18·4 g., 73%), n_D^{25} 1·4342 (Whitmore, Mosher, Adams, Taylor, Chapin, Weisel, and Yanko, *J. Amer. Chem. Soc.*, **1944**, **66**, 725, give n_D^{20} 1·4356).

Attempted Reaction of Vinyl Cyanide with Arylamines.—(i) An equimolecular mixture of vinyl cyanide and aniline was refluxed at 180° for 1·5 hr. Distillation afforded only the starting materials (90% recovery); no residue remained. (ii) Vinyl cyanide (5·3 g., 1·5 mols.) and *p*-anisidinium chloride (10·65 g., 1 mol.) were heated under reflux at 180° for 1·5 hr. The cold mixture was washed with acetone (10 c.c.) and ether (40 c.c.), leaving unchanged *p*-anisidinium chloride (10·4 g.), m. p. and mixed m. p. undepressed. The filtrates left no residue of b. p. >100°.

N-2-*Cyanoethyl*-p-*anisidine.*—(i) A mixture of 2-diethylaminoethyl cyanide (12·6 g., 1·5 mols.) and *p*-anisidinium chloride (10·65 g., 1 mol.) was heated under reflux at 180° for 1·5 hr. On cooling, addition of acetone (10 c.c.) gave diethylammonium chloride (5·2 g., 95%), which when washed with acetone and ether had m. p. and mixed m. p. 218—220°. Distillation of the filtrate gave two fractions: (1) b. p. 84—106°/3 mm. (3·1 g.), containing 2-diethylaminoethyl cyanide (2·25 g.) and *p*-anisidine (0·85 g., 10%, estimated as the acetyl derivative); (2) b. p. 136—150°/0·001 mm. (9·45 g., 78%), needles, m. p. and mixed m. p. 62—64°, of *N*-2-cyanoethyl-*p*-anisidine.

(ii) A mixture of diethylamine (7·3 g., 1·5 mols.), vinyl cyanide (5·3 g., 1·5 mols.), and *p*-anisidinium chloride (10·65 g., 1 mol.) was heated under reflux at 180° for 1·5 hr. Working up as in (i) gave diethylammonium chloride (6·3 g., 86%), m. p. and mixed m. p. 218—220°, and distillation gave two fractions: (1) b. p. 65—120°/2 mm. (5·8 g.), containing 2-diethylaminoethyl cyanide (3·95 g.) and *p*-anisidine (1·8 g., 22%); (2) b. p. 136—150°/0·001 mm. (7·9 g., 68%), m. p. and mixed m. p. 62—64°, of *N*-2-cyanoethyl-*p*-anisidine.

(iii) An experiment identical with (ii) but extending over 2·5 hr. gave 15% of recovered *p*-anisidine and 76% of *N*-2-cyanoethyl-*p*-anisidine.

(iv) A mixture of vinyl cyanide (8 g., 1·5 mols.), diethylammonium chloride (10·95 g., 1 mol.), and *p*-anisidine (12·3 g., 1 mol.) was refluxed at 180° for 1·5 hr. The cooled mixture was treated with sodium hydroxide solution and extracted with chloroform. Distillation of the dried extracts gave three fractions: (1) unchanged 2-diethylaminoethyl cyanide and *p*-anisidine; (2) b. p. 140—150°/0·001 mm. (14 g., 79%), m. p. and mixed m. p. 62—64°, of *N*-2-cyanoethyl-*p*-anisidine; (3) b. p. 180°/0·001 mm. (1·6 g., 7%), of *NN*-di-(2-cyanoethyl)-*p*-anisidine, m. p. 103—104°, as needles from alcohol (Braunholtz and Mann, *J.*, **1953**, 1817, give m. p. 103°).

(v) A mixture of vinyl cyanide (5·3 g., 1·5 mols.), *p*-anisidine (8·2 g., 1 mol.), and diethylammonium benzenesulphonate (1·54 g., 0·1 mol.) was heated under reflux at 180° for 1·5 hr. The cooled melt, treated as in (i), gave diethylammonium benzenesulphonate (0·35 g., 22%), m. p. and mixed m. p. 137—139°. Distillation gave two fractions: (1) b. p. 94—110°/2 mm. (2·6 g., 32%), of *p*-anisidine, m. p. and mixed m. p. 55—57°; (2) b. p. 135—145°/0·001 mm. (6·85 g., 59%), of *N*-2-cyanoethyl-*p*-anisidine (mixed m. p.).

N-*Deuterodiethylamine.*—Diethylamine (4·2 c.c., 1 mol.) was added to a stirred solution of ethylmagnesium bromide (from 9·6 g. of magnesium) in ether (135 c.c.), and the mixture refluxed for 0·5 hr. The ether was distilled off, and di*iso*amyl ether (100 c.c.) added simultaneously. The cooled (ice) reaction mixture was decomposed by addition of deuterium oxide (12 g., 1·5 mol., 99·7% D_2O). Distillation through a column (6″ × ¾″) filled with single-turn glass helices gave *N*-deuterodiethylamine, b. p. 52—56°/760 mm., in 50% yield.

1-Deutero-2-diethylaminoethyl Cyanide.—Prepared by reaction of equimolar quantities of *N*-deuterodiethylamine and vinyl cyanide, this had b. p. 100—101°/30 mm., n_D^{17} 1·4350.

Reaction with p-anisidinium benzenesulphonate. The above cyanide (2·7 g., 1·5 mols.) and *p*-anisidinium benzenesulphonate (4 g., 1 mol.) were heated under reflux for 1·5 hr. at 180°. Cooling and addition of dry acetone (2 c.c.) gave diethylammonium benzenesulphonate which was filtered off and washed with dry acetone (2 c.c.) and dry ether (5 × 5 c.c.) Distillation of the filtrate gave (after a first fraction containing recovered cyanide and *p*-anisidine) *N*-2-cyanoethyl-*p*-anisidine, b. p. 135—140°/0·001 mm., solidifying to white needles.

Spectroscopic Technique.—The spectra were obtained with a double-beam infrared spectrometer based on the " optical null " principle, constructed by one of us (R. L. W.), and with sodium chloride optics. Calibration was effected in the usual manner by means of Oetjen, Kao, and Randall's data (*Rev. Sci. Instr.*, 1942, **13**, 515). Solids were examined as mulls in hexachlorobutadiene. and liquids as capillaries or in a 0·050-cm. cell.

Mass-spectrometric Technique.—Mass-spectra were measured with a Consolidated 21-103 mass-spectrometer. No spectra were available to check the purity of the diethylamine and *N*-deuterodiethylamine. Both samples contained a small quantity of an unidentified impurity with a peak at mass 86, but it was assumed that this impurity did not interfere with the peaks at masses 72, 73, and 74 used in the analytical calculations. The further assumption was made that the sensitivity (mass-spectrometer deflection per unit of pressure) was the same for the parent peak (73) of $NHEt_2$ as for that (74) of $NDEt_2$. The *N*-deuterodiethylamine sample was then found to contain at least 80% of $NDEt_2$ and a comparison of the ratio of the 72 and the 73 peak in the $NHEt_2$ sample with the 73/74 ratio in the $NDEt_2$ sample showed that the impurity in the latter was not $NHEt_2$. Similarly, the $NEt_2{\cdot}CH_2{\cdot}CHD{\cdot}CN$ was at least 80% pure, although, in this case, the impurity could have been $NEt_2{\cdot}CH_2{\cdot}CH_2{\cdot}CN$.

The presumed diethylammonium benzenesulphonate, when treated with sodium hydroxide solution, gave $NHEt_2$ with a mass-spectrum almost identical with that of the original sample of diethylamine. The sensitivity of the mass-spectrometer was such that 2% of $NDEt_2$ would have been detected if present in this sample. As a further check, the water formed in the reaction of the benzenesulphonate with alkali was examined for deuterium content but none was found. This shows that deuterium could not have been lost from the amine salt by exchange with the water present.

The authors are grateful to Professor C. K. Ingold, F.R.S., for helpful discussion.

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The Structure of Lapachenole, a Hardwood Extractive.

By R. Livingstone and M. C. Whiting.

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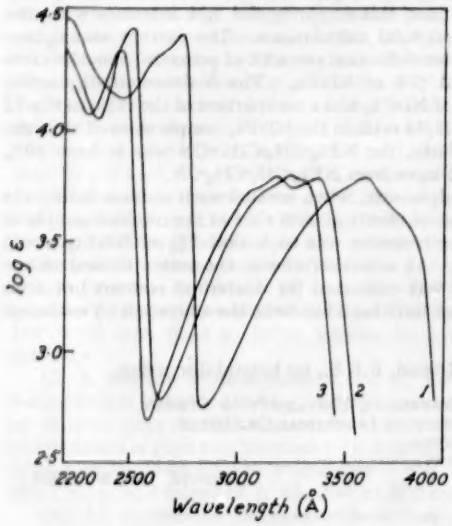
The name " lapachenole " is proposed for a substance present in the wood of " Brazilian white peroba." Its structure has been elucidated as 4′-methoxy-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran (III), and confirmed by the total synthesis of its dihydro-compound.

Because of reports that use of the hardwood " Brazilian white peroba " (*Paratecoma alba*) was causing dermatitis, an attempt was made to isolate the active constituent. The (active) neutral fraction of the light petroleum extract yielded a compound, $C_{16}H_{16}O_2$, m. p. 62°, which appeared to be identical with a substance isolated by Manuelli (*Atti Acad. Lincei*, 1900, **9**, 102, 314; 1913, **22**, 686, see *Chem. Zentr.*, 1900, II, 727; 1901, I, 114; 1914, I, 984) from " lapacho wood," probably the same species and given the Italian trivial name " lapachonon." The structure (III) now established for this compound, for which we propose the less confusing English name " lapachenole," is related to 1-methoxynaphthalene, which Katz (see *Chem. Abs.*, 1946, **40**, 7525) found to cause a similar dermatitis; it may therefore be the active factor, though tests were inconclusive.

Lapachenole proved to be inert towards lithium aluminium hydride, whence both of the oxygen atoms must be present in ether groupings. A Zeisel determination indicated one methoxyl group, and catalytic hydrogenation gave a crystalline dihydro-compound, which had an ultraviolet absorption spectrum considerably different from that of lapachenole and generally similar to that of some naphthalene derivatives. Distillation of lapachenole with zinc dust gave naphthalene, the yield (3%) being, if anything, higher than that obtained from lapachol in a comparable experiment. Lapachenole was therefore believed to have an ethylenic linkage in conjugation with a naphthalene nucleus; this view was confirmed when more vigorous hydrogenation gave a liquid, but apparently homogeneous, hexahydro-derivative with an absorption spectrum ($\lambda_{max.}$ 2950 Å, $\varepsilon = 3600$) very like that of quinol ($\lambda_{max.}$ 2880 and 3000 Å, $\varepsilon = 2300$), allowance being made for nuclear alkylation. Resemblances to catechol, resorcinol, and phenol, and their ethers were less pronounced. Accordingly, 1 : 4-dimethoxynaphthalene was prepared for comparison with dihydrolapachenole, with results which leave no doubt about the chromophore present in the latter (see Figure). Hydrogenation of 1 : 4-dimethoxynaphthalene also gave a (crystalline) tetrahydro-derivative (5 : 8-dimethoxytetralin) which in its ultraviolet absorption spectrum closely resembled hexahydrolapachenole.

Ultraviolet spectra of (1) *lapachenole,* (2) *dihydrolapachenole, and* (3) 1 : 4-*dimethoxynaphthalene.*



Oxidative degradation of lapachenole had been extensively employed by Manuelli (*locc. cit.*), who used nitric acid and bromine in most of his experiments, obtaining products involving nuclear substitution, together with oxalic and phthalic acid.

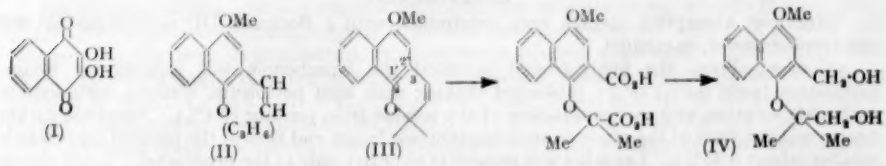
Treatment of lapachenole with potassium permanganate in acetone gave a dibasic acid $C_{16}H_{16}O_6$ (yield *ca.* 40%), in addition to phthalic acid and a trace of pigment identified almost with certainty as *iso*-naphthazarin (I). This reaction can only be explained plausibly as the oxidation of $-CH{:}CH-$ to two carboxyl groups. Whereas lapachenole and its dihydro-compound (and also 1 : 4-dimethoxynaphthalene) had given deep red syrups on treatment with hydrogen bromide in acetic acid, the acid $C_{16}H_{16}O_6$ underwent smooth dealkylation at 60°, giving, however, a mixture of 1 : 4-dihydroxynaphthalene-2-carboxylic acid and its 4-monomethyl ether which were not easily separable. After further transformations the latter was isolated as such and as its methyl ester, and the former as 1 : 4-diacetoxynaphthalene. Partial structure (II) could now be written.

The nature of the C_3H_6 bridge—for biogenetic reasons an *iso*propylidine grouping was of course suspected—was proved by reduction of the methyl ester of the acid $C_{16}H_{16}O_6$ to the diprimary glycol with lithium aluminium hydride. In hot 30% sulphuric acid this underwent a pinacolinic rearrangement, giving *iso*butaldehyde in 75% yield, isolated as its 2 : 4-dinitrophenylhydrazone. The only *primary* aryloxy-alcohol which could have given this aldehyde is (IV), derived from (III) as the structure for lapachenole.

Attention was now directed to the confirmation of this structure (III) by synthesis of the dihydro-compound. Preliminary attempts to condense 4-methoxy-1-naphthol with isoprene in the presence of zinc chloride (cf. Smith, Ungnade, Hoehn, and Wawzonek, *J. Org. Chem.*, 1939, **4**, 311) proved unsuccessful. Condensation with 1-bromo-3-methylbut-2-ene (Smith and Denyes, *J. Amer. Chem. Soc.*, 1936, **58**, 304; Smith and Dobrovolny, *ibid.*, 1926, **48**, 1693) was then attempted in benzene at 80° in the presence of zinc chloride. From the syrupy neutral fraction a picrate was readily obtained which

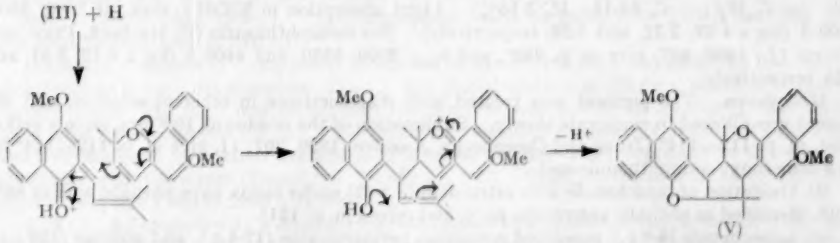
proved to be identical with that of dihydrolapachenole, and this substance was obtained from it on chromatography.

Subsequently to the investigations described, more complete infrared data became available for lapachenole and its dihydro-derivative which confirm the relation between them here postulated. Bands common to both spectra include those at 1645 cm.$^{-1}$, similar



to one in the spectrum of quinol dimethyl ether, and at 760 cm.$^{-1}$, characteristic of benzenoid rings with four adjacent positions unsubstituted. The chief differences were in the intensity of absorption at 3050 cm.$^{-1}$, significantly greater for lapachenole than its dihydro-compound, and in the strong band at 684 cm.$^{-1}$ in the spectrum of lapachenole but absent in that of the dihydro-compound. Both may be attributed to the *cis*-CH:CH grouping.

The high-melting substance, m. p. 258°, formed on treatment of lapachenole with acids was stated by Manuelli (*locc. cit.*) to be dimeric, on the basis of both cryoscopic and ebullioscopic measurements which gave molecular weight values between 350 and 500. On the other hand, molecular weights of 245, 290, 296, and 255 (cf. 240 required by $C_{16}H_{16}O_2$) were obtained in replicate determinations (ebullioscopic, in benzene) using the accurate method of Menzies (*J. Amer. Chem. Soc.*, 1921, **43**, 2309); a monomeric formula was therefore assumed during much of the present work. It could be explained with the assumption that a Wagner–Meerwein rearrangement had given a 2 : 3-dimethyl-2-chromen system, provided that considerable stabilising influences were ascribed to C–H hyperconjugation and crystal-lattice forces—the substance is almost insoluble in common solvents. In a conversation with one of us (M. C. W.), Professor R. B. Woodward criticised this formulation, and, since no other monomeric structure was plausible, suggested that it must be dimeric. The use of both isothermal distillation (Niederl *et al.*, *Science*, 1940, **92**, 225; 1944, **100**, 228) and ebullioscopic measurements in benzene by Pregl's method ("Die quantitative organische Mikroanalyse," Springer, Berlin, 1930, p. 237) then clearly indicated that the compound was indeed dimeric. No evidence could be obtained for the presence of an ethylenic linkage; thus its ultraviolet and infrared absorption spectra closely resemble those of dihydrolapachenole, it was inert to potassium permanganate in acetone at 56°, and on hydrogenation it absorbed four mols. of hydrogen (assuming $M = 480$) very slowly to give a high-melting product resembling hexahydrolapachenole in its ultraviolet absorption. These facts suggest a heptacyclic structure; Professor Woodward's formula, (V), represents the most satisfactory of several alternatives, being the only heptacyclic dimer whose formation can be envisaged without the intervention of carbonium ions.



A 2 : 4-dinitrophenylhydrazone was obtained from lapachenole by Professor D. H. R. Barton (personal communication); it is formed only under forcing conditions, and then

in small yield. Subsequent experiments (Livingstone, unpublished work) have shown that comparable reactions occur with authentic chromens, and the formation of this derivative, whose structure will be discussed later, therefore need not be considered as evidence for, *e.g.*, a vinyl ether grouping in the molecule.

Experimental

Ultraviolet absorption spectra were determined with a Beckman DU or Unicam SP 500 spectrophotometer, in ethanol.

Isolation.—From the finely-ground sapwood the lapachenole was isolated by steam-distillation (yield 0·5%) or by prolonged shaking with light petroleum, washing with sodium carbonate solution, and recrystallisation of the residue from pentane (0·4%). From the darker heartwood the yield of the crude neutral fraction was larger and that of the purified lapachenole smaller (about 0·35%). Lapachol was present in quantity only in the heartwood. Lapachenole formed plates, m. p. 62°, from light petroleum (Found : C, 80·2, 80·45; H, 6·55, 6·65. Calc. for $C_{16}H_{16}O_3$: C, 80·0; H, 6·65%). When adsorbed on alumina lapachenole becomes photo-sensitive, giving initially an orange colour which later becomes deep blue-green.

Lapachenole picrate was prepared from methanolic solutions of the components; it formed violet needles, m. p. 141° [Found : C, 56·5; H, 4·1; *M* (by titration), 470, 472, 468. $C_{22}H_{19}O_9N_3$ requires C, 56·3; H, 4·05; *M*, 469].

Dihydrolapachenole.—Lapachenole (5·0 g.), platinic oxide (0·1 g.), and ethanol (100 c.c.) were shaken in hydrogen until absorption (1 mol.) was complete. Filtration, evaporation, and recrystallisation from aqueous ethanol gave *dihydrolapachenole* (3·75 g.), m. p. 78° (Found : C, 79·0; H, 7·25. $C_{16}H_{18}O_3$ requires C, 79·3; H, 7·45%). It formed a *picrate* (in methanol), violet needles, m. p. 141° (Found : C, 56·45; H, 4·3; N, 8·75. $C_{22}H_{21}O_9N_3$ requires C, 56·1; H, 4·45; N, 8·9%).

Hexahydrolapachenole.—Lapachenole (0·50 g.), platinic oxide (0·08 g.), and glacial acetic acid (25 c.c.) were shaken together under hydrogen until (after 33 hr.) the rate of absorption became negligible; the uptake was about 3 mols. Filtration, addition of water, and isolation of the neutral fraction gave a syrup which was distilled at 10^{-5} mm., to give *hexahydrolapachenole* (0·39 g.), $n_D^{17\cdot5}$ 1·5668 (Found : C, 77·9; H, 8·75. $C_{16}H_{22}O_3$ requires C, 78·0; H, 8·95%). Light absorption : flat maximum, 2910—2980 Å (ε = 3640).

In another experiment equal weights of lapachenole and platinic oxide were shaken in hydrogen in acetic acid for 60 hr., whereafter uptake ceased (total, *ca.* 5 mols.). The product was a heterogeneous liquid which still absorbed appreciably around 2600 Å (Found : C, 79·0; H, 10·3; OMe, 8·8. Calc. for $C_{16}H_{28}O_3$, *i.e.*, a dodecahydro-derivative : C, 76·2; H, 11·1; OMe, 12·3%).

Oxidation of Lapachenole.—(*a*) A solution of lapachenole (2 g.) in acetone (50 c.c.) was treated with potassium permanganate (13 g.). After 24 hr. at 20° acetone (450 c.c.) was added and the mixture was heated under reflux for 3 hr., cooled, and filtered. The residue was suspended in water (350 c.c.), acidified with dilute sulphuric acid, and treated with sulphur dioxide to give a clear yellow solution. This was extracted continuously with ether, and the ether was evaporated, giving an orange gum (1·54 g.) from which, after addition of ether, phthalic acid (0·11 g.; m. p. and mixed m. p. 190—196°) was separated. When the ethereal solution was washed with aqueous sodium hydroxide it was decolorised, a blue-green colour appearing in the lower layer; acidification of the latter gave a bright red solid (40 mg.) which sublimed at 258—260° after recrystallisation from ethyl acetate (Found : C, 62·15; H, 3·5; OMe, nil. Calc. for $C_{10}H_6O_4$: C, 63·15; H, 3·15%). Light absorption in EtOH : max. at 2680, 3300, 4400 Å (log ε 4·32, 3·32, and 3·26, respectively). For *iso*naphthazarin (I), Macbeth, Price, and Winzor (*J.*, 1935, 327) give m. p. 280°, and $\lambda_{max.}$ 2700, 3350, and 4400 Å (log ε 4·12, 3·31, and 3·25, respectively).

Methylation. The pigment was treated with diazomethane in ethereal solution, and the solvent was allowed to evaporate slowly. Sublimation of the residue at 10^{-6} mm. gave a yellow solid, m. p. 112—114° (Zinke and Ossenbecke, *Annalen*, 1899, **307**, 11, give m. p. 112—114° for 2 : 3-dimethoxy-α-naphthaquinone).

(*b*) Oxidation of lapachenole with nitric acid (*d* 1·12) under reflux gave phthalic acid in 80% yield, identified as phthalic anhydride, m. p. and mixed m. p. 131°.

(*c*) Lapachenole (6·0 g.), powdered potassium permanganate (17·4 g.), and acetone (150 c.c.) were heated under reflux for 6 hr., cooled, and filtered, the residue being washed with acetone and dried. Water (200 c.c.) was added and sulphur dioxide was introduced until the manganese

dioxide had dissolved. An orange residue remained, and was filtered off, dried, washed with benzene, and crystallised from aqueous ethanol, giving α-(*2-carboxy-4-methoxy-1-naphthoxy*)*iso-butyric acid* (2·2 g.) as prisms, m. p. 163—164° (Found: C, 63·0; H, 5·3%; equiv., 151. $C_{16}H_{16}O_6$ requires C, 63·1; H, 5·25%; equiv., 152). Light absorption: max. at 2470, 3060, and 3380 Å (log ε 4·46, 3·72, and 3·60 respectively). Decomposition at 170° in nitrogen liberated 1·03 mol. of carbon dioxide, estimated gravimetrically.

Dealkylation of this acid was effected with hydrogen bromide in acetic acid (25 c.c.; 50%) under reflux at 60—65° under nitrogen in 3 hr. On cooling, a grey solid (0·6 g.), m. p. 190—193° (decomp.), separated; crystallisation from aqueous ethanol gave needles (*A*), m. p. 200° (decomp.), displaying a blue fluorescence in ethanol and yielding a green colour with ferric chloride (Found: C, 64·7; H, 4·2; OMe, 4·95. Calc. for a mixture of 1 : 4-dihydroxy-2-naphthoic acid and its monomethyl ether (ratio 2 : 1): C, 65·15; H, 3·95; OMe, 4·9%).

1 : 4-*Diacetoxynaphthalene*.—The above mixture (*A*) (200 mg.), acetic anhydride (5 c.c.), and sodium acetate (100 mg.) were heated under reflux for 2 hr. Addition of water, isolation of the neutral fraction, and crystallisation from aqueous ethanol gave 1 : 4-diacetoxynaphthalene (40 mg.), m. p. and mixed m. p. 130·5—131·5°.

Methyl 1-Hydroxy-4-methoxy-2-naphthoate.—(*a*) The above mixture (*A*) (100 mg.) in ether (7 c.c.) and methanol (2 c.c.) was treated with an excess of diazomethane. The solution was washed with dilute hydrochloric acid and sodium hydroxide solution (to remove the dihydroxy-ester), then evaporated, and the residue (10 mg.) was crystallised from aqueous ethanol, then acetone, giving the hydroxy-ester, m. p. 136—137° (Homeyer and Wallingford, *J. Amer. Chem. Soc.*, 1942, **64**, 801, give m. p. 137—138°).

(*b*) The mixed acids (85 mg.) were dissolved in methanol (5 c.c.), and the solution was saturated with hydrogen chloride. The mixture was heated under reflux for 90 min. and poured into water, and the precipitate was collected; this was shaken with ether and sodium hydrogen carbonate solution. Acidification of the aqueous layer and isolation with ether gave 1-hydroxy-4-methoxy-2-naphthoic acid (50 mg.), m. p. 196—200° [Homeyer and Wallingford, *loc. cit.*, give m. p. 196—198° (decomp.)]. The neutral fraction was crystallised from aqueous acetone, giving the corresponding methyl ester (20 mg.), m. p. 137—138°.

2-(*2-Hydroxymethyl-4-methoxy-1-naphthyloxy*)-*2-methylpropan-1-ol* (IV).—The C_{16} acid (1·2 g.) was dissolved in ether (20 c.c.) and methanol (15 c.c.), and treated with an excess of diazomethane in ether for 60 min. The solvent was removed, and the residue was dissolved in dry ether and added with stirring to an excess of ethereal lithium aluminium hydride. After 2 hours' heating under reflux the excess of hydride was decomposed and the neutral fraction was isolated with ether; crystallisation from light petroleum (b. p. 80—100°) gave the *diol* (0·81 g.) as needles, m. p. 105—106° (Found: C, 69·3; H, 7·5. $C_{16}H_{20}O_4$ requires C, 69·55; H, 7·25%).

iso*Butaldehyde*.—The above glycol (153 mg.) and 30% sulphuric acid (55 c.c.) were heated under reflux while a stream of nitrogen was passed through the boiling liquid and up the condenser into a methanolic solution of 2 : 4-dinitrophenylhydrazine sulphate. After chromatography and crystallisation the derivative which separated (102 mg., 75%) formed yellow needles, m. p. 183—184°, undepressed on admixture with *iso*butaldehyde 2 : 4-dinitrophenylhydrazone.

Lapachenole Dimer (V ?).—This substance is obtained whenever lapachenole is subjected to acidic conditions. Conveniently, lapachenole (5·0 g.) and formic acid (150 c.c.; *d* 1·12) were heated to 90°; the ether dissolved and, after a few minutes, the dimer began to separate. After 30 min. the mixture was cooled and the *product* collected and crystallised from ethyl acetate, giving needles (4·25 g.), m. p. 258° (Found: C, 79·7; H, 6·7; OMe, 13·85. $C_{32}H_{32}O_4$ requires C, 80·0; H, 6·65; OMe, 12·9%). Light absorption: max. at 2500, 3220, 3330 Å (ε 37,900, 6290, and 5660, respectively, in $CHCl_3$).

Octahyrod-derivative of Lapachenole Dimer.—The dimer (190 mg.) was dissolved in a mixture of chloroform (7 c.c.), ethyl acetate (25 c.c.), and glacial acetic acid (25 c.c.), added in that order. Platinic oxide (330 mg.) was added and the mixture was shaken in hydrogen until uptake (*ca.* 4 mols.) was complete (24 hr.). Filtration and isolation of the neutral *product* gave a solid which crystallised from ethyl acetate as prisms, m. p. 248—249°, depressed to 224—225° on admixture with the dimer (Found: C, 78·65; H, 8·15. $C_{32}H_{40}O_4$ requires C, 78·7; H, 8·2%). Light absorption: max. 2900 Å (ε 6500).

1 : 2 : 3 : 4-*Tetrahydro-5 : 8-dimethoxynaphthalene*.—1 : 4-Dimethoxynaphthalene (467 mg.), glacial acetic acid (40 c.c.), and platinic oxide (42 mg.) were shaken in hydrogen until absorption (uptake *ca.* 2 mols.) was complete (24 hr.). Isolation of the neutral fraction and recrystallisation from methanol gave the *tetrahydro-ether* (370 mg.) as plates, m. p. 43—44° (Found: C,

75·1; H, 8·2. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). Light absorption: max. at 2870 Å (ε 3250). A shoulder at 3180 Å indicated the presence of 7% of unreduced dimethoxynaphthalene.

4-Methoxy-1-naphthol.—1 : 4-Dihydroxynaphthalene (from 1 : 4-naphthaquinone, cf. *Org. Synth.*, Coll. Vol. I, 2nd Edn., **49**, 383) (12·1 g.) in methanol (40 c.c.) was refluxed in nitrogen with sodium hydroxide (3·4 g.) and methyl iodide (12·1 g.) for 4 hr. Evaporation of the solvent gave a brown solid which darkened rapidly in air; it was at once sublimed at 10^{-4} mm., giving at 90° a fraction (2·1 g.) consisting mainly of 1 : 4-dimethoxynaphthalene, and at 90—112° a solid (5·47 g.), m. p. 120—125°, which was crystallised from light petroleum (b. p. 80—100°), giving 4-methoxy-1-naphthol (3·15 g., 24%), m. p. 124—125°. Russig (*J. prakt. Chem.*, 1900, **62**, 50) gives m. p. 124—125°.

Synthesis of Dihydrolapachenole.—The above phenol (0·2 g.), 1-bromo-3-methylbut-2-ene (170 mg.), zinc chloride (170 mg.), and benzene (6 c.c.) were heated under reflux for 3 hr. The cooled benzene solution was washed with dilute hydrochloric acid, sodium hydroxide, and sodium hydrosulphite (dithionite) solution, and finally water, then evaporated. The residue was treated with saturated methanolic picric acid, and the precipitate was crystallised from methanol, giving dihydrolapachenole picrate (160 mg.), m. p. and mixed m. p. 141—142·5°. This was dissolved in ether and decomposed chromatographically, giving dihydrolapachenole (56 mg.), m. p. and mixed m. p. 78°. The greater part of the methoxynaphthol used was recovered from the alkaline hydrosulphite washings.

At an early stage in this work Professor D. H. R. Barton, F.R.S., informed us that he also had begun investigations on what proved to be lapachenole, and had obtained from it a 2 : 4-dinitrophenylhydrazone and a picrate; we thank him for resigning the problem to us and giving us his preliminary results. We thank Professor E. R. H. Jones, F.R.S., for practical assistance and valuable advice. We are indebted to Dr. Robert Murray, H.M. Inspector of Factories, for directing our attention to this problem and helping us to obtain peroba wood, to the Forest Products Research Laboratory for a generous gift of lapachenole, to Messrs. E. M. Morton and H. Swift for microanalyses, to Mrs. E. B. Bates for ultraviolet spectroscopic data, and to Dr. D. Meakins for infrared data.

THE UNIVERSITY, MANCHESTER. [*Received, April 1st*, 1955.]

Researches on Acetylenic Compounds. Part LI. The Syntheses of γ-Methyleneglutamic Acid and γ-Methyleneglutamine.*

By P. C. WAILES and M. C. WHITING.

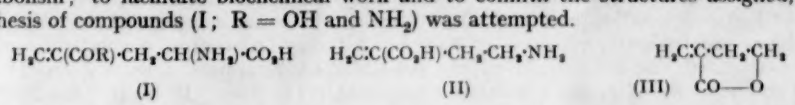
[Reprint Order No. 6289.]

The structures proposed for γ-methyleneglutamic acid and for γ-methyleneglutamine are confirmed by rational syntheses of the racemic acids. The routes employed render these substances readily accessible.

RECENTLY the isolation of an amino-dicarboxylic acid and its half-amide from ground-nut seedlings was described (Done and Fowden, *Biochem. J.*, 1952, **51**, 451). These compounds, the main ninhydrin-active substances present, were assigned structures (I; R = OH and NH_2, respectively), and their presence has since been reported in hops (Harris, *Chem. and Ind.*, 1954, 244) and in tulip bulbs (Zacharius, Pollard, and Steward, *J. Amer. Chem. Soc.*, 1954, **76**, 1961). The corresponding α-keto-acids occur in tulip leaves (Towers and Steward, *ibid.*, p. 1959), and also in ground-nut seedlings (Fowden and Webb, *Biochem. J.*, 1955, **59**, 228). In the latter plant, these acids play an important role in nitrogen transport (*idem*, *Ann. Bot.*, 1954, **18**, 72, 417). The decarboxylation product from the acid (I), *i.e.*, the monocarboxylic acid (II), occurs in ground-nut seedlings (Fowden and Done, *Biochem. J.*, 1953, **55**, 548), and the closely related lactone (III) was isolated by Cavallito and Haskell (*J. Amer. Chem. Soc.*, 1946, **68**, 2332) from *Erythronium americanum*. There is thus some evidence that α-methylene-acids of this type are of importance in plant

* Part L, *J.*, 1955, 1874.

metabolism; to facilitate biochemical work and to confirm the structures assigned, the synthesis of compounds (I; R = OH and NH_2) was attempted.

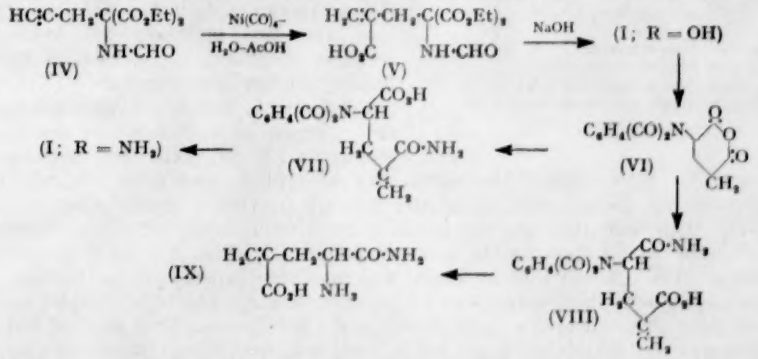


Diethyl 1-formamidobut-3-yne-1 : 1-dicarboxylate (IV) (Gershon, Meek, and Dittmer, *ibid.*, 1949, **71**, 3573) was treated with nickel carbonyl in aqueous-ethanolic acetic acid (Jones, Shen, and Whiting, *J.*, 1950, 230); a typical exothermal reaction took place, and the Reppe carboxylation product (V) was formed in 45% yield. Vigorous alkaline hydrolysis, followed by the removal of sodium ions by passage through ZeoKarb-216 resin, gave an acidic solution, which was evaporated. Extraction of the residue with alcohol removed the *N*-formyl derivative of (I; R = OH), leaving the free amino-acid (I; R = OH) undissolved: the former probably arose by re-formylation during the isolation.

Natural γ-methyleneglutamic acid is probably the L-isomer, although its optical activity has not yet been reported. On treatment with mineral acid it gives the racemate, best distinguished by the lower yield of carbon dioxide given on enzymic decarboxylation (Fowden, personal communication). Both acids of natural origin soften at about 204°, as did the synthetic acid, and no depression was observed on admixture; the racemic acids of natural and synthetical origin gave identical *X*-ray powder diagrams and identical and detailed infrared spectra as Nujol suspensions. In addition, the three amino-dicarboxylic acid specimens were inseparable chromatographically.

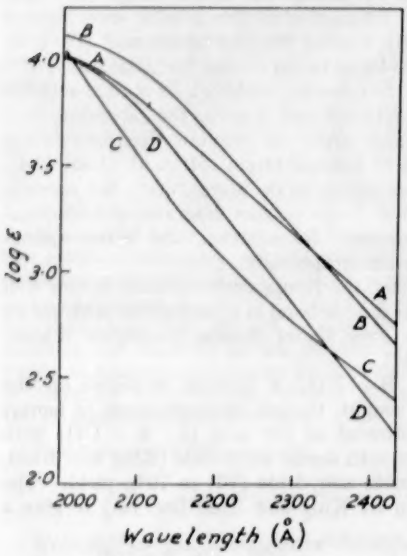
The synthetic method employed is rational, since the Reppe carboxylation is now well documented (Reppe, *Annalen*, 1953, **582**, 1) and the double bond in α-methylene-acids shows no tendency to rearrange into the main chain even under drastic conditions (Cason, Allinger, and Williams, *J. Org. Chem.*, 1953, **18**, 842).

For the preparation of the half-amide (I; R = NH_2) a method modelled on the conversion of glutamic acid into glutamine was sought, though hydrogenolysis of benzyl groups obviously could not be employed. Treatment of the acid (I; R = OH) with phthalic anhydride in pyridine, and subsequently with acetic anhydride (King and Kidd, *J.*, 1949, 3315), gave the corresponding phthalimido-anhydride (VI) in 70% yield. The analogous derivative of glutamic acid was shown by King and Kidd (*loc. cit.*) to give a



74% yield of the phthaloylglutamine on treatment with ammonia in dry ether–dioxan, although some of the isomeric half-amide may have been formed and eliminated by crystallisation. In the present case, the carbonyl group on which attack by ammonia was desired is conjugated with the methylene group, and lower reactivity, relative to the carbonyl group adjacent to the phthalimido-grouping, is therefore to be expected. The product, obtained in excellent yield and analytically satisfactory, melted at 189—190°, not sharpened by repeated crystallisation. Removal of the phthaloyl group (see below) gave a deliquescent amorphous solid from which no homogeneous product could be isolated. It was concluded that a mixture of amides (VII) and (VIII) has been obtained,

and, since crystallisation had failed to separate it, counter-current partition between butan-1-ol and a saturated phosphate buffer (pH 6·2) was investigated, fractions being analysed spectrophotometrically at 3000 Å. Although concentrated solutions, initially supersaturated, had to be employed, the available 24-tube apparatus readily separated the two components. The slower-moving component (47% from VI), m. p. 203—205°, had pK 5·18 in 60% ethanol (cf. 4·93 for phthalimidoacetic acid in the same solvent), and was clearly the desired half-amide (VII). The other isomer (20% from VI), m. p. 201—204°, had pK 5·99, agreeing well with pK 6·38 for methacrylic acid, under the same conditions, when allowance is made for the acid-strengthening effects of the phthalimido- and amino-carbonyl groups, and was therefore (VIII). The ultraviolet absorption spectra were almost identical; infrared spectra were different but not diagnostically useful, because of the multiplicity of bands in the 1600—1800-cm.$^{-1}$ region.



A, *γ-Methyleneglutamine* (I; R = NH_2).
B, *Glycine plus methacrylamide.*
C, *γ-Methyleneisoglutamine* (IX).
D, *Glycine amide plus methacrylic acid.*
(*All in* H_2O.)

Treatment of the phthaloyl derivative (VII) with hydrazine in neutral aqueous solution at 20° (King and Kidd, *loc. cit.*) and isolation of the methanol-insoluble portion of the product gave a crystalline half-amide (A) in 24% yield. In boiling ethanol (Sheehan and Corey, *J. Amer. Chem. Soc.*, 1952, **74**, 4555) phthalhydrazide was formed in good yield, but no crystalline amino-acid could be isolated. It was now necessary to prove (*a*) that (A) was the racemic half-amide (I; R = NH_2), and (*b*) that, apart from optical isomerism, it was identical with the natural half-amide. From analytical data, and from its ultraviolet absorption spectrum, which at least proved that the $H_2C{=}\overset{|}{C}{\cdot}\overset{|}{C}{=}O$ chromophore was present, (A) must be either (I; R = NH_2) or the isomer (IX). Assuming, from the pK measurements that the two phthaloyl half-amides were correctly identified, the method of formation barely permits the structure (IX), though rearrangements through cyclic intermediates are common in derivatives of succinic and glutaric acids (cf., *inter al.*, Battersby and Robinson, *J.*, 1955, 259). The ultraviolet absorption spectrum (Figure), though indecisive, agrees better with the model mixture (glycine + methacrylamide) for (I; R = NH_2) than with that (glycine amide + methacrylic acid) for (IX). Nevertheless attempts were made to prepare the authentic isomer (IX) from the less acidic phthaloyl-half-amide. The reaction with hydrazine was much less satisfactory in this case, giving amorphous products which were shown by paper chromatography to be complex mixtures; however, after several weeks a small quantity of crystalline material was isolated. This substance was very soluble and could not be freed from inorganic contaminants, but paper chromatography indicated that only one substance was present capable of giving a colour with ninhydrin or with chlorine followed by potassium iodide and starch (Rydon and Smith, *Nature*, 1952, **169**, 922). Dr. L. Fowden (personal communication) confirmed that it was separable from (A) chromatographically, and also found that it gave a substance inseparable from γ-methyleneglutamic acid on acid hydrolysis. Its ultraviolet absorption spectrum agrees with that expected for the amide (IX), and we conclude that it was in fact a specimen of the latter, containing about 20% of inorganic salts. Since the two phthaloyl-amides thus give different products with hydrazine, it may be assumed that no rearrangement is involved, and that (A) is therefore the isomer (I; R = NH_2).

The proof that this was the racemate corresponding to the natural amide was obtained indirectly, since powder *X*-ray patterns were quite different, and the infrared spectra of the two specimens (perforce determined in Nujol suspensions) differed so profoundly that scepticism in other respects seemed essential. Paper chromatography and enzymic hydrolysis were employed, with results, detailed in a preliminary publication (Wailes, Whiting, and Fowden, *Nature*, **1954**, **174**, 130), which leave no doubt as to the chemical identity of the two substances. As might be expected, the isomeric amide (IX) did not undergo enzymic hydrolysis.

In earlier attempts to synthesise these compounds, 2-aminopent-4-ynoic acid (Gershon, Meek, and Dittmer, *loc. cit.*) proved to be inert to nickel carbonyl (cf. the similar unreactivity of pent-4-ynoic acid; Jones, Whitham, and Whiting, *J.*, **1954**, 1865). Its phthaloyl derivative was prepared and converted into a well-crystallised methyl ester which, despite satisfactory analytical data and a normal infrared spectrum, melted over a 10° range. This ester reacted exothermally with nickel carbonyl, but the acidic product did not crystallise.

Experimental

M. p.s were determined on the Kofler block. Ultraviolet absorption data were determined with a Unicam SP 500 spectrophotometer, and infrared spectra with a Perkin–Elmer double-beam Model 21 spectrophotometer. Dissociation constants (quoted as pK_a) were determined with a pH meter (Cambridge Instrument Co. Ltd.) and are probably accurate to $\pm 0{\cdot}05$.

Diethyl 3-Carboxy-1-formamidobut-3-ene-1 : 1-dicarboxylate (V).—Diethyl 1-formamidobut-3-yne-1 : 1-dicarboxylate (Gershon, Meek, and Dittmer, *loc. cit.*) (115 g.) was heated, with stirring, in ethanol (500 c.c.), water (30 c.c.), and acetic acid (75 c.c.) at 65°. Nickel carbonyl (40 g., 30 c.c.) under ethanol (10 c.c.) was added dropwise and after an initial induction period a typical exothermal ("Type A") reaction began (Jones, Shen, and Whiting, *J.*, **1951**, 48). The temperature rose to 75° and the colour changed to bright green. The temperature was maintained at 70—75° by addition of nickel carbonyl and when reaction had ceased ether (*ca.* 100 c.c.) was added and the excess of carbonyl was removed by distillation of all material boiling below 50°. The residue was poured into dilute sulphuric acid and extracted with ether, the acid fraction being isolated through potassium hydrogen carbonate. Crystallisation from benzene–light petroleum (b. p. 60—80°) afforded the *α-methylene-acid* (61·5 g., 45%) as leaflets, m. p. 140—144° (Found: C, 50·2; H, 5·8; N, 5·15. $C_{12}H_{17}O_7N$ requires C, 50·15; H, 5·95; N, 4·9%).

γ-Methyleneglutamic Acid (I; R = OH).—The above acid (53 g.) was heated in a solution of sodium hydroxide (40 g.) in water (800 ml.) under reflux for 4·5 hr. After cooling, an equal volume of water was added and the sodium was removed by passage through ZeoKarb-216 (activated with 2N-hydrochloric acid; 6 × 52 cm.). Elution with water was continued until the pH of the eluate had risen to 5. The whole of the eluate (*ca.* 6 l.) was evaporated under reduced pressure to 600 c.c., then treated with charcoal and evaporated further. Crystallisation then soon commenced and the product was collected by alternate filtration and evaporation. When the volume had been reduced to 100 c.c., 20 g. of a white solid had been isolated (material collected subsequently was highly coloured and impure, and was discarded). The equivalent weight of the solid was considerably lower than that of the desired acid, so it was extracted with boiling ethanol (100 c.c.). A white crystalline residue (13·0 g., 45%) of DL-γ-methyleneglutamic acid (I; R = OH) remained. This was sufficiently pure to use in the next stage (equiv., 155. Calc. for $C_6H_9O_4N$: equiv., 159), and had m. p. 204° (softens) (Done and Fowden, *loc. cit.*, give softening point 204° with the same rate of heating). For analysis it was recrystallised from water as small prisms softening at 204° (Found: C, 44·95; H, 5·35; N, 8·6%; equiv., 158. Calc. for $C_6H_9O_4N$: C, 45·3; H, 5·7; N, 8·8%). Evaporation of the ethanol extract gave a crystalline residue (5·5 g.) which appeared to be the *formyl derivative* [Found: equiv., 93·3. $C_5H_7ON(CO_2H)_2$ requires equiv., 93·5], and was not investigated further.

Phthaloyl-γ-methyleneglutamic Anhydride (VI).—γ-Methyleneglutamic acid (13·0 g.) and phthalic anhydride (12·5 g.; recrystallised from acetic anhydride) were boiled together in dry pyridine (200 c.c.) for 7·5 hr. The solvent was evaporated under reduced pressure, leaving a viscous oil which dissolved in warm acetic anhydride (100 c.c.); the solution was heated on the steam-bath for a further 10 min. On cooling, colourless leaflets of the *anhydride* (VI) [15·5 g., 70% from (I; R = OH)] separated, having m. p. 222—224° (Found: C, 62·2; H, 3·55; N, 5·2.

$C_{14}H_9O_5N$ requires C, 62·0; H, 3·35; N, 5·15%). The infrared spectrum showed bands at 970 and 1630 cm.$^{-1}$ (characteristic of $CH_2{:}CR{\cdot}CO$) and carbonyl bands at 1706, 1755, 1774, and 1804 cm.$^{-1}$.

Phthaloyl-γ-methylene-glutamine (VII) *and* -*isoglutamine* (VIII).—The anhydride (VI) (15·5 g.) was dissolved in warm dry dioxan (200 c.c.), and an excess of anhydrous ammoniacal ether was added slowly with shaking and occasional cooling, the ammonium salts of the half-amides separating. After 15 min. the solid was filtered off, dissolved in the minimum of water (*ca.* 40 c.c.), and acidified to Congo-red with 5N-hydrochloric acid. After several hours at 0° the separated solid (14·7 g., 89%) was collected; it had m. p. 189—196°, not improved by repeated crystallisation from water or aqueous acetone.

Countercurrent partition separation. The mixed phthalimido-amides (4·0 g.) were dissolved in butanol (80 c.c.) which had been equilibrated with M-phosphate buffer solution (pH 6·2) and introduced in 40-c.c. portions into the first two tubes of a 24-tube countercurrent partition apparatus (see Craig and Craig in Weissburger, "Technique of Organic Chemistry," Vol. III, New York, 1950). The lower layer in each tube consisted of 80 c.c. of the above buffer solution, and two fractions of butanol were transferred through the apparatus just ahead of the amide solution to ensure complete saturation of the aqueous layer. Fractions of the upper phase were collected by the single-withdrawal technique until spectroscopic analysis at 3000 Å showed that the faster-moving amide was being eluted from the apparatus. The upper phases of all of the tubes were then analysed spectroscopically at 3000 Å.

Phthaloyl-γ-methyleneglutamine (VII). The contents of tubes 1—7 were combined and the lower layer was acidified with phosphoric acid and extracted with the upper. After being washed with a little water, the butanol layer was evaporated under reduced pressure and the residue was crystallised twice from aqueous methanol, giving prisms (2·1 g., 47% from the anhydride) of the *half-amide*, m. p. 203—205° (Found: C, 58·05; H, 4·0; N, 10·1. $C_{14}H_{12}O_5N_2$ requires C, 58·35; H, 4·2; N, 9·7%). The infrared spectrum (Nujol suspension) included bands at 1638, 948, and 968 cm.$^{-1}$ and carbonyl bands at 1664, 1714, and 1780 cm.$^{-1}$. In 60% ethanol at 15° the pK was 5·18.

Phthaloyl-γ-methyleneisoglutamine (VIII). Tubes 13—24 were worked up similarly. Two crystallisations from aqueous methanol afforded needles (0·9 g., 20% from the anhydride) of the *amide*, m. p. 201—204° (Found: C, 58·05; H, 4·2; N, 9·5%). The infrared spectrum (Nujol suspension) showed bands at 932, 966, and 1630 cm.$^{-1}$, and carbonyl peaks at 1706 and 1775 cm.$^{-1}$. The pK in 60% ethanol at 15° was 5·99.

γ-Methyleneglutamine (I; R = NH_2).—Phthaloyl-γ-methyleneglutamine (VII) (1·6 g.) was dissolved in aqueous sodium carbonate (0·30 g. in 10 c.c. water), and hydrazine hydrate (1 mol., 0·56 c.c. of a solution containing 0·495 g. per c.c.) was added. The mixture was kept at room temperature for 3 days, then acidified with 5N-hydriodic acid and cooled to 0° for several hours. Phthalhydrazide was removed and the filtrate was neutralised (pH meter) with 5% sodium carbonate solution and evaporated almost to dryness at 40° (bath-temp.). Dry methanol (*ca.* 50 c.c.) was then added and the solution was cooled to −10° for 24 hr. On filtration *γ-methyleneglutamine* (0·21 g., 24%) was obtained as colourless plates, m. p. 171—173° (decomp.), unchanged on recrystallisation (Done and Fowden, *Biochem. J.*, 1952, **51**, 451, give m. p. 173° for the naturally occurring amide) (Found: C, 45·55; H, 6·15; N, 17·65. $C_6H_{10}O_3N_2$ requires C, 45·55; H, 6·35; N, 17·7%).

γ-Methyleneisoglutamine (IX).—Phthalolyl-γ-methyleneisoglutamine (VIII) (0·80 g.) was treated as above, and the crude amide was precipitated from the mixture with sodium iodide by trituration with absolute ethanol. Chromatography of the residue in butanol–acetic acid–water (Partridge, *Biochem. J.*, 1948, **42**, 238) and development with chlorine and starch–iodide (Rydon and Smith, *loc. cit.*) showed the presence of four compounds of different R_F values. Attempted crystallisation from aqueous methanol, propan-2-ol, or acetone did not effect purification, but when an aqueous-ethanol solution was kept for several weeks a small quantity (35 mg.) of crystalline material separated (m. p. 174°) (Found: N, 13·8%). Appreciable amounts of inorganic contaminants were still present, but paper chromatography gave only one spot after development with ninhydrin (reddish-brown) or with chlorine–potassium iodide.

2-Phthalimidopent-4-ynoic Acid.—2-Aminopent-4-ynoic acid (0·72 g.) (Gershon, Meek, and Dittmer, *loc. cit.*) and phthalic anhydride (0·92 g., 1 mol.) were heated under reflux in pyridine (10 ml.) for 2 hr. The solution was evaporated under reduced pressure, the residue was taken up in benzene, and the acid fraction was isolated. Crystallisation from benzene–light petroleum (b. p. 60—80°) gave the *acid* (0·96 g., 62%) as needles, m. p. 158—161° (Found: C, 63·95; H, 4·15; N, 5·9. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·75; N, 5·75%). The *methyl ester*, prepared in

methanol (13 ml.) containing concentrated sulphuric acid (0·15 ml.) at 20° for 48 hr., crystallised from aqueous methanol as needles, m. p. 97—107°, not sharpened by recrystallisation (Found : C, 65·2; H, 4·4; N, 5·4. $C_{14}H_{11}O_4N$ requires C, 65·35; H, 4·3; N, 5·45%).

We are indebted to Dr. L. Fowden for samples of the natural amino-acids, for advice on chromatographic procedures, and especially for the careful comparative experiments involving the two half-amides. We also thank Dr. J. Done and Professor E. R. H. Jones, F.R.S., for their interest and advice, Professor K. Lonsdale, F.R.S., for *X*-ray powder comparisons, and Dr. L. J. Bellamy for infrared data on the natural and the synthetic specimens of (I; R = OH and NH_2). We acknowledge a maintenance grant from the Commonwealth of Australia Scientific Research Organisation to one of us (P. C. W.), and thank Messrs. E. S. Morton and H. Swift for microanalyses and Miss W. Peadon and Mrs. J. Hopkins for ultraviolet and infrared data.

THE UNIVERSITY, MANCHESTER, 13. [*Received, April 1st,* 1955.]

The Reaction of Chlorodimethyl Ether with Ethanol and with Ethoxide Ions.

By P. BALLINGER, P. B. D. DE LA MARE, G. KOHNSTAM, and B. M. PRESTT.

[Reprint Order No. 6421.]

The reaction of chlorodimethyl ether has been studied in ethanol, and in mixtures of ethanol and diethyl ether, with and without added lithium chloride, lithium ethoxide, and other electrolytes. Evidence is presented that the solvolyses are unimolecular, and at least about 10^{14} times faster than the corresponding reaction of methyl chloride; and that the reactions in the presence of ethoxide ions are substantially bimolecular, and some 10^5 times faster than the corresponding reaction of methyl chloride.

CHLORODIMETHYL ETHER and its analogues very readily undergo reactions in which the halogen is displaced by a nucleophilic reagent. It is commonly supposed that such reactions are unimolecular (S_N1), since the methoxyl group would be expected to facilitate reaction by this mechanism, through its power of mesomeric release towards the developing carbonium ionic centre. It is not clear, however, whether such an effect might also facilitate bimolecular nucleophilic substitution. Leimu and Salomaa (*Acta Chem. Scand.*, 1947, **1**, 353) have examined the alcoholysis of chlorodimethyl ether and related compounds. In ethanol as solvent, they recorded that the rate, though fast, is measurable, and that the reaction is accelerated by added sodium ethoxide. They concluded that the solvolysis is unimolecular, but that reaction in the presence of added base contains a bimolecular (S_N2) component.

These authors also examined the reactions of α-chloro-ethers with small quantities of ethanol in dioxan. They found that hydrogen chloride catalyses the reaction, and supported a mechanism due to Bohme (*Ber.*, 1941, **74**, 248), whereby catalysis was determined by addition of a proton to the oxygen atom of the chloro-ether :

$$RO{\cdot}CH_2Cl + H^+ \longrightarrow RHO^+{\cdot}CH_2{\cdot}Cl \xrightarrow[ROH]{} RO{\cdot}CH_2{\cdot}OR + H^+ + H^+ + Cl^-$$

In media of such low ionising capacity, however, the formal order of the reaction with respect to added catalysts of this sort is not necessarily a measure of the molecularity of the reaction (cf. Gelles, Hughes, and Ingold, *J.*, 1954, 2918). Salomaa (*Annales Universitatis Turkuensis*, 1953, A, XIV *) recently has adopted the view that catalysis by added hydrogen chloride in the alcoholysis of chloro-ethers is in fact the result of a primary salt effect.

The present experiments have been carried out largely with solvents of low ionising

* We are indebted to Dr. Salomaa for drawing our attention to this publication, and for interesting discussions.

capacity, so that the rates should be conveniently measurable. The effects of added ethoxides have been examined in solvents of widely differing ionising power, and have been compared with the effects of other added salts; for further comparison, the reactions of acetyl chloride and of triphenylchloromethane have been studied in outline under the least ionising of the conditions employed.

Experimental

Materials.—Chlorodimethyl ether, prepared from methanol, formaldehyde, and hydrogen chloride, and purified by careful fractional distillation, had b. p. 58·8—59·0°/761 mm., and was almost completely free from dissolved hydrogen chloride. Triphenylchloromethane, recrystallised from benzene, had m. p. 111—112°. Acetyl chloride, purified by fractional distillation, had b. p. 50·8—51·0°/760 mm. 2-Chloroethyl methyl ether, b. p. 93°/758 mm., was prepared as described by Jones and Power (*J. Amer. Chem. Soc.*, 1924, **46**, 2531), and 1-chloroethyl methyl ether, b. p. 70—72°/710 mm., as described by Henze and Murchison (*ibid.*, 1931, **53**, 4077). Ethanol was dried by Manske's method (*ibid.*, p. 1106). Diethyl ether was dried over sodium wire, and distilled, with precautions to avoid the entry of water. A solvent described as "*x*%" ether refers to a mixture of *x* ml. of ether and (100 − *x*) ml. of ethanol, measured at room temperature. Lithium chloride was dried by heating it in a current of dry air. Solutions of the various ethoxides were obtained by dissolving the appropriate metal in the solvent. The radioactive materials and methods have been described elsewhere (de la Mare and Vernon, *J.*, 1954, 2504).

Kinetics.—Conventional methods were used for the kinetic measurements. The following details exemplify the general features. The solvent (*ca.* 60 ml. of 50% ether containing 0·064N-lithium chloride) was brought to thermostat temperature (0·0°) in a volumetric flask. Chlorodimethyl ether was added and, at intervals, samples (5·0 ml.) were pipetted into neutralised acetone which had been cooled to below −50°, and were titrated with 0·0303N-sodium ethoxide in ethanol (lacmoid as indicator). Results were:

Time (min.)	0·38	1·15	2·33	3·80	5·80	9·13	16·07	∞
Titre (ml.)	1·08	2·12	3·68	5·40	7·19	9·86	13·23	17·18
k_1 (min.$^{-1}$)	—	0·093	0·093	0·093	0·089	0·091	0·090	—

Stable end-points were obtained by this technique, and the constancy of the first-order rate-coefficients, illustrated above, was typical of all the solvolytic measurements. Reactions with added ethoxide were followed by pipetting the samples into acetone, cooled to below −50°, to which had been added a small proportion (usually not more than 5% by volume) of standard aqueous hydrochloric acid, in measured amount, in excess of that required to neutralise the ethoxide in the sample, which was then back-titrated with ethanolic sodium ethoxide in the usual way. The results shown in the Tables are, for mutual comparison, given as first-order rate-coefficients, calculated (by the usual formula) on the disappearance of organic chloride. For runs with added ethoxide ion, therefore, since these were of second-order form, the first-order coefficients refer to initial values, obtained by extrapolation to zero time. Rate-coefficients obtained by the above methods are as follows.

In 90% ether. (*a*) Chlorodimethyl ether; (i) at 25·0°; 10^4k_1 (sec.$^{-1}$) = 0·69; +0·018M-LiCl, 3·3; +0·25M-LiCl, 19·3; +0·015M-LiOEt, 3·6; +0·022M-LiOEt, 4·8; +0·018M-$LiClO_4$, 2·6; +0·008M-NaOEt, *ca.* 40 (falling); (ii) at 0·0°: 10^4k_1 = 0·089; +0·0066M-$NaClO_4$, 0·25; +0·034M-LiCl, 0·57; +0·020M-NaOEt, 12 (falling); +0·010M-KOEt, 9·5 (falling). (*b*) Acetyl chloride, at 25·0°: (i) 10^4k_1 = 8·8; +0·018M-LiCl, 11·5; (ii) at 0·0°, +0·022M-LiOEt, >150. (*c*) Triphenylchloromethane at 25°: 10^4k_1 = 1·04; +0·25M-LiCl, 1·24; +0·02M-NaOEt, *ca.* 4 (falling). (*d*) 1-Chloroethyl methyl ether: reaction too fast to be measured at 0°.

In 50% ether. Chlorodimethyl ether, at 0·0°: 10^4k_1 = 12·3; +0·062M-LiCl, 15·3; +0·106M-LiCl, 16·8; +0·073M-LiOEt, 62 (falling); +0·139M-LiOEt, 127 (falling); +0·068M-NaOEt, 88 (falling).

In ethanol. (*a*) Chlorodimethyl ether, at 0·0°: 10^4k_1 = 142; +0·124M-LiCl, 147; +0·151M-LiOEt, 570 (falling); +0·066M-NaOEt, 450 (falling). (*b*) 2-Chloroethyl methyl ether underwent solvolysis negligibly slowly in this solvent even at 90°: a very slow solvolysis ($k_1 \geqslant 3 \times 10^{-6}$ sec.$^{-1}$) could be detected in 50% aqueous ethanol at the latter temperature.

Subsidiary experiments showed that the product of reaction between chlorodimethyl ether

and ethanol in mixtures of diethyl ether and ethanol was that of nucleophilic displacement of chloride; none of the product of the possible reaction $X \curvearrowright Me{-}O{-}CH_2{-}Cl \curvearrowright$ was detected in either the presence or the absence of chloride ions.

The exchange reaction between chlorodimethyl ether and lithium chloride labelled with ^{36}Cl was studied in outline in the following way. Samples were pipetted into cold acetone and brought to neutrality (lacmoid) with standard alkali. The acetone and the chlorodimethyl ether were then evaporated at low temperature; negligible further acidity developed. The specific radioactivity of the lithium chloride residue was then determined in the usual way. The velocity coefficients were determined by the formulæ:

$$k_1 = bk_2 = \frac{2{\cdot}303b}{t(a+b)} \log_{10}\left\{\frac{1}{1 - x(1 + b/a)/c}\right\}$$

Here the symbols have the usual significance (cf. de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930). The results are in Table 1.

TABLE 1. *Exchange reactions between chlorodimethyl ether and* $^{36}Cl^-$.

Solvent	Temp.	a	b	t (min.)	Acidity of sample (M)	c	$c - x$	10^4k_1 (sec.$^{-1}$)
90% Ether	0·0°	0·0275	0·0336	3·59	0·00045	176·1	122·8	26
Acetone	−4·5	0·0834	0·0204	3·60	0·00095	93·9	19·3	*ca.* 60,000

Conductance Measurements.—The conductances of some of the electrolytes used in the kinetic measurements were measured at 25° using audio-frequency alternating current and conventional apparatus. The cell-constant was 0·264 cm.$^{-1}$. Measurements were made by successive dilutions of a stock sample of known concentration. Results obtained in ethanol for sodium ethoxide, lithium ethoxide, and lithium chloride were in reasonable accordance with those of the more detailed investigations made by White (*J.*, 1928, 1413), Jones and Hughes (*J.*, 1934, 1197), and Copley, Murray-Rust, and Hartley (*J.*, 1930, 2492). The conductances in 50% ether were measured similarly. Values for the most dilute solutions were obtained in the following way. To the solvent (25 ml., contained in the cell) were added, by means of a carefully calibrated 0·1-ml. graduated pipette, successive portions of *ca.* 0·025N-solutions of the salts in the solvent, and the resistances were measured after each addition. The quoted equivalent conductances of ethoxides are not corrected for the conductance of the solvent, since the self-ionisation of ethanol is repressed in the presence of ethoxide ions. The results are not considered to be sufficiently precise to justify attempted correction for the presence of dissolved impurities; such corrections, discussed by Jones and Hughes (*loc. cit.*), are small except at the highest dilutions.

Conductances at 25° in 50% ether. c *in mole l.*$^{-1}$.

NaOEt. *Solvent, R* = 422,000 *ohms.*											
10^4c	811	325	65·0	32·5	12·2	7·68	6·50	3·76	2·78	1·47	0·98
R (Ω)	817	1733	4376	6520	11590	15850	19000	27260	34930	47300	92000
Λ_c	4·0	4·7	9·2	12·2	18·7	21·7	21·4	25·8	27·2	28·3	29·2
LiOEt. *Solvent, R* = 411,000 *ohms.*											
10^4c	948	379	75·8	37·9	16·8	11·3	7·60	3·79	2·57	1·30	
R (Ω)	1124	2208	5844	8790	13600	17210	21990	34530	44600	72100	
Λ_c	2·5	3·1	5·9	7·9	11·6	13·6	15·8	20·2	23·0	28·3	
LiCl. *Solvent, R* = 410,000 *ohms.*											
10^4c	743	149	37·1								
R (Ω)	469	1387	3314								
Λ_c	7·6	12·8	21·5								

The following are the results for the resistances of a 0·005N-solution of sodium ethoxide in ether containing different proportions of ethanol at 25°:

Ethanol (%)	10	13·5	19·6	25·0	30	43·5
Resistance (ohms) ...	3,260,000	1,000,000	210,000	76,200	28,530	7880

The very rapid decrease in conductance with decreasing proportion of ethanol probably results largely from a decrease in the energy of solvation, and consequent increase in ion-pair

formation, combined with a decrease in the equivalent conductance at infinite dilution. Ionisation of the electrolytes is very small when the solvent contains less than 30% of ethanol, though these values are likely to be inaccurate because alternating-current methods are not suitable for the precise measurement of such high resistances.

In estimating the limiting slope expected on the Onsager theory for 50% ether, the dielectric constant is assumed to be 13·6 (cf. King and Patrick, *J. Amer. Chem. Soc.*, 1921, **43**, 1835), and the viscosity is taken as 0·00472 c.g.s. unit. The latter was determined by using a conventional Ostwald viscometer, with ethanol (viscosity assumed to be 0·108 c.g.s. unit) as a standard of reference. The value obtained similarly for ether (0·00263 c.g.s. unit) is in good agreement with accepted values.

Discussion

The Effect of the Methoxyl Group on Reactivity by the S_N1 Mechanism.—Although the solvolysis of chlorodimethyl ether in pure ethanol is very rapid, it is not too fast to be measured. The rate-coefficient, obtained in the present investigation ($10^4k_1 = 142$ sec.$^{-1}$ at 0·0°) by following the production of acid, is in good agreement with that ($10^4k_1 = 152$ sec.$^{-1}$) derived by a short extrapolation of Leimu and Salomaa's data (*loc. cit.*); the latter value was obtained by following the unchanged chlorodimethyl ether, titrated as formaldehyde after alkaline hydrolysis. The increased rate observed in the presence of added base is small when compared with the magnitude of the increase expected when reaction with the solvent is bimolecular (cf. Hughes, Ingold, Masterman, and McNulty, *J.*, 1940, 899), so it can be concluded with confidence that the sovolysis is essentially unimolecular.

The rate of ethanolysis of chlorodimethyl ether is considerably reduced when the solvent is changed to 50% ether ($10^4k_1 = 12·3$ sec.$^{-1}$ at 0·0°) and to 90% ether ($10^4k_1 = 0·089$ sec.$^{-1}$ at 0·0°). Application of the same type of criterion as was used for the work in ethanol as solvent determines that in the less ionising solvents the solvolyses are unimolecular also. For the solvent containing 90% of ether, conductance measurements indicate that added electrolytes exist almost entirely as ion-pairs; as a check, therefore, the effect of added base on the rate of solvolysis of acetyl chloride was measured also, since this compound would be expected to react by a second-order (presumably bimolecular) process (cf. Brown and Hudson, *J.*, 1953, 3352) in the presence of an effective nucleophilic reagent. Added lithium ethoxide very powerfully accelerated the sovolysis of acetyl chloride; it accelerated the solvolysis of chlorodimethyl ether only by a relatively small factor, and hardly had any effect on the rate of solvolysis of triphenylchloromethane. Hence it is considered that the solvolyses of the last two compounds are unimolecular even in 90% ether. On this basis, comparison of the reactivity of chlorodimethyl ether and triphenylchloromethane shows that the methoxyl substituent, in its power of facilitating heterolysis of the C–Cl system, is roughly equivalent to three phenyl groups. It is, of course, very much more effective than three methyl groups; *tert.*-butyl chloride undergoes solvolysis in ethanol at 44·6° with a velocity coefficient of $1·33 \times 10^{-6}$ sec.$^{-1}$ (de la Mare and Vernon, unpublished measurements), some 5×10^6 times less rapidly than chlorodimethyl ether ($k_1 = 0·7$ sec.$^{-1}$ at 44·6°, by extrapolation of Leimu and Salomaa's data).

Further structural comparisons of some interest can be made indirectly. The rates of S_N1 solvolyses of other compounds (cf. de la Mare and Vernon, *J.*, 1954, 2504) are usually increased by a factor of about 5×10^3 by change from ethanol to 50% aqueous ethanol. The rate of solvolysis of chlorodimethyl ether in 50% aqueous ethanol would on this basis be about 71 sec.$^{-1}$ at 0°, and about $0·5 \times 10^7$ sec.$^{-1}$ at 90°. The rate of solvolysis of 2-chloroethyl methyl ether at 90° is certainly not greater than about 10^{-7} sec.$^{-1}$ (cf. Experimental section), and hence the α-, as compared with the β-methoxyl substituent, has increased the rate of solvolysis by a factor of between 10^{13} and 10^{14} or thereabouts.* Similarly, since chlorodimethyl ether is about 7×10^4 times more reactive in ethanol than 3 : 3-dimethylallyl chloride, which itself is some 4×10^8 times more reactive than *n*-propyl chloride (de la Mare and Vernon, *loc. cit.*; Vernon, *J.*, 1954, 423), it may be concluded that

* "Neighbouring-group" participation of the β-hydroxyl substituent is regarded by Winstein (*Bull. Soc. chim., France*, 1951, **18**, 55) as providing only about 1 kcal./mole of "driving force" for the solvolyses of such compounds.

chlorodimethyl ether is probably at least 10^{13} times more reactive than *n*-propyl chloride, and hence (cf. Bateman and Hughes, *J.*, 1940, 945) probably 10^{14} times more reactive, by the S_N1 mechanism, than methyl chloride.

The extremely large effect of the α-methoxyl substituent must be attributed to conjugation of the group with the developing carbonium ionic centre, and may be represented :

$$MeO{-}CH_2{-}Cl \longrightarrow MeO{=}CH_2\ Cl \longrightarrow [MeO{-}\overset{+}{C}H_2 \longleftrightarrow MeO{=}\overset{+}{C}H_2] + Cl^-$$

The following structural comparisons concerning the unimolecular reactions of chloroethers can now be made, using results of the present investigation in conjunction with those obtained by Leimu and Salomaa (*loc. cit.*) and by Salomaa (*loc. cit.*) :

Compound	MeO·CHMeCl	Me·CH_2·O·CH_2Cl	MeO·CH_2Cl	EtO·CH_2·O·CH_2Cl	$(CH_2Cl)_2O$
Rel. rate of solv....	>100	3	1	0·003 *	0·0001

Introduction of a second electron-donating group (the methyl group) directly on the reacting carbon atom increases reactivity so much that the rate of solvolysis cannot be measured at 0°, even in 90% ether. When introduced into the methoxyl substituent, the methyl group increases, whereas ethoxyl or chlorine considerably reduces, the rate of unimolecular solvolysis. Presumably these groups act by altering inductively the availability of the lone pair of electrons on the oxygen atom of the activating substituent. Similar effects, though rather smaller, have been recorded by Bradfield, Brynmor Jones, and their co-workers (cf. Bradfield, *Trans. Faraday Soc.*, 1941, **37**, 726) for the activating influences in aromatic halogenation of substituted methoxyl groups.

Salt Effects in the Unimolecular Solvolysis of Chlorodimethyl Ether.—Unimolecular solvolyses are facilitated by increase in the ionising power of the environment, so increase in the ionic strength of the solution should increase the rate of the reaction : this is in accordance with the observations. The magnitude of the influence of added salts would be expected to increase as the dielectric constant and ionising power of the solvent diminished, and the following results illustrate this point :

Solvent	Ethanol	50% Ether	90% Ether
Dielectric constant	23·0	13·6 †	6·0 †
Equivalent conductance ($\Lambda_{0.01N}$)	24·5	6·0	~0·01
Rate of solvolysis of chlorodimethyl ether, in the presence of 0·02N-lithium chloride, relative to rate in the absence of added salt	1·01	1·08	5·1

The effect of added lithium or sodium perchlorate on the rate in 90% ether is of the same order of magnitude as that found for lithium chloride.

Although the rate of solvolysis of chlorodimethyl ether in 90% ether increases linearly and rapidly with the lithium chloride concentration, it would be incorrect to conclude that, in the lithium chloride-catalysed solvolysis, either the chloride or the lithium ion participated covalently in the rate-determining process. The influence of these ions is, in our view, essentially a matter of ion-atmosphere stabilisation of the transition state, and is particularly large in the present instance, because of the low ionising power of the solvent.‡ A similar consideration applies to the effect of added hydrogen chloride, investigated by Leimu and Salomaa and by Böhme (*locc. cit.*) in similar solvents. In these cases also, the influence of hydrogen chloride may be the result of a primary salt-effect, or could be the result of electrophilic catalysis of the heterolysis of the C–Cl bond (cf. Gelles, Hughes, and Ingold, *loc. cit.*). The special interpretation, proposed by Böhme (*loc. cit.*), which makes catalysis depend on attachment of the proton to the oxygen atom of the methoxyl group,

* Estimated by Salomaa (*loc. cit.*) from the rate of release of the second chlorine atom in the ethanolysis of bischloromethyl ether.

† Estimated from the dielectric constant of ether (4·2; International Critical Tables).

‡ The structure of the cationic intermediate is also of importance. The solvolysis of triphenylchloromethane is accelerated much less powerfully than that of chlorodimethyl ether, as may be explained by the relatively large size of the triphenylmethyl cation, since dispersion of charge over such a large volume must considerably reduce the forces of solvation.

is unnecessary.* It is, of course, theoretically likely that attachment of a proton would inhibit, rather than catalyse, the heterolysis of the C–Cl bond.

Bimolecular Reactions of Chlorodimethyl Ether.—Leimu and Salomaa (*loc. cit.*) concluded that, in ethanol, added sodium ethoxide increases the rate of reaction of chlorodimethyl ether through the incursion of a bimolecular (S_N2) reaction. The experiments recorded above are in agreement with this view. Although the rates are rather too fast for accurate measurement, it is clear that lithium chloride, which from its conductance appears to be more dissociated than lithium ethoxide, has very little influence on the rate of the solvolysis, whereas both lithium and sodium ethoxide increase the rate of the reaction considerably.

Similar conclusions can be reached from consideration of the results obtained by using 50% ether as solvent. Rates therein were more conveniently measurable, and variation in the concentration of lithium ethoxide proved the second-order character of the reaction.

The annexed Table gives second-order rate-coefficients, obtained by calculating as first-order coefficients the rate of disappearance of chlorodimethyl ether, extrapolating these rates to zero reaction, subtracting the rate of the concomitant solvolysis, and dividing by the initial concentration of ethoxide:

Second-order rate-coefficients for reactions of chlorodimethyl ether with ethoxides.

Solvent	Ethanol	50% Ether	90% Ether
k_2 (NaOEt, 0·0°; l. mole^{-1} sec.$^{-1}$)	0·47	0·11	0·06
k_2 (LiOEt, 0·0°; l. mole^{-1} sec.$^{-1}$)	0·30	0·07	Very small

Bimolecular reactions between ions and neutral molecules are usually faster in a less ionising solvent. Vernon (*loc. cit.*), however, showed that for allylic chlorides, the change in rate with solvent is often in the opposite direction. He associates this behaviour with an abnormally high polarity of the transition state, resulting essentially from mesomeric release of electrons from the vinyl substituent. The methoxyl group is electronically similar, and releases electrons very much more powerfully. An abnormal solvent effect might, therefore, be expected also in the case of chlorodimethyl ether.

There is another factor which deserves consideration in this connection, namely, the effect that could be attributed following such treatments as that of Evans and Sugden (*J.*, 1949, 270) to incomplete dissociation of the electrolytes. The results of Copley *et al.* (*loc. cit.*) for the conductances of very dilute solutions of sodium ethoxide in ethanol show small negative deviations from the slope required by the Onsager theory. Such deviations have been interpreted (cf. Ogston, *Trans. Faraday Soc.*, 1936, **32**, 1679) as resulting from ion-pair formation; for this electrolyte in this solvent the effect seems to be rather small. Lithium ethoxide, however, gives consistently greater deviations from the Onsager theory (cf. Jones and Hughes, *loc. cit.*), and this, taken in conjunction with the consistently lower second-order rate-coefficients observed with this salt, suggests that at least a part of these differences may be attributed to incomplete dissociation of lithium ethoxide.

Our results suggest that the situation is very similar in 50% ether. The results for sodium ethoxide suggest that the initial slope of the plot of Λ_c against $c^{\frac{1}{2}}$ is not considerably greater than that required by the Onsager theory ($\Lambda_c = \Lambda_0 - 383c^{\frac{1}{2}}$, on the assumptions given above). Hence sodium ethoxide is probably not much more associated in this solvent than in ethanol.

It is concluded, therefore, that the results in the Table may exaggerate the effect of the solvent on the observed second-order rate coefficients, but that correction for incomplete

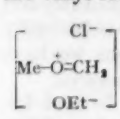
* It should be noted also that changes in the rate of reaction which depend on changes in the proportion of a reactive and relatively ionising species (*e.g.*, ethanol) added to a relatively non-ionising solvent cannot be treated satisfactorily by calculating the apparent order of the reaction with respect to the ionising component from the change in rate with concentration of the latter. Such changes in rate are properly to be considered as effects resulting from changes in the medium, and are not necessarily a reflection of the number of molecules of the reactive component participating through covalency changes in the transition state.

dissociation would probably not alter the direction of change, namely, decrease in rate with decreasing ionising power.

The measurements of conductance in 90% ether suggest that the electrolytes under these conditions must exist very largely as uncharged species. Indeed, it is questionable whether in this solvent the solutes are behaving as electrolytes at all; their observed influences on the rates of reaction may arise essentially from dipolar interactions between the reactants and ion-pairs or neutral molecules. The specific influences of different ethoxides could also result from bimolecular reactions involving these formally uncharged species, or from electrophilic catalysis of the heterolysis.

The Effect of the Methoxyl Group on Reactivity by the S_N2 Mechanism.—Vernon (*loc. cit.*) measured the rate and activation energy for the reaction of *n*-propyl chloride with ethoxide ions in ethanol. Extrapolation to 0° gives a rate coefficient of $k_2 = 2{\cdot}4 \times 10^{-8}$ l. mole^{-1} sec.$^{-1}$. Methyl chloride would be expected to react about a hundred times faster than *n*-propyl chloride under these conditions (cf. Dostrovsky and Hughes, *J.*, 1946, 157). Hence chlorodimethyl ether must be rather more than 10^5 times more reactive than methyl chloride by the S_N2 mechanism.

Although the effect of the methoxyl group is in this case much smaller than that of the same group in the S_N1 mechanism, it is still very considerable and requires discussion. The effects of substituents on the rates of bimolecular substitution are difficult to predict in any specific case, since electron-release facilitates breaking of the C–Cl bond but inhibits attack by a nucleophilic reagent. There is some evidence, however, that groups which have their influence on the rate mainly through conjugative, rather than inductive, processes, generally facilitate bimolecular reactions of this type. Hughes, Ingold, and Shapiro (*J.*, 1936, 225) discussed this matter in relation to the effect of the phenyl substituent, and more recently Vernon (*loc. cit.*) has discussed the effect of the α-vinyl group in accelerating the rate of bimolecular nucleophilic substitution. The conjugative power of the methoxyl group is, as has been observed above, much greater than that of the vinyl substituent, and hence the former group has a considerable influence on the rate of bimolecular substitution. In the valence-bond representation, the annexed structure contributes to the transition state for the bimolecular reaction of chlorodimethyl ether; no similar structure of corresponding importance can be written for methyl chloride.



The exchange reactions between chlorodimethyl ether and chloride ion have been investigated only in outline. Reaction in acetone was almost, but not quite, complete in 3·6 min., and an estimate of the rate-coefficient indicates that chlorodimethyl ether is more reactive than methyl chloride (de la Mare, *J.*, 1955, 3169) in this solvent by a factor of 10^5. As this estimate accords with the value indicated above for reaction with ethoxide ion, the presumption is that the exchange reaction is bimolecular in this solvent, and it seems likely that this could be tested by kinetic measurements at lower temperatures. The exchange in 90% ether is much faster than the accompanying solvolysis, and therefore also may be bimolecular, but in this solvent a kinetic test would probably be difficult to interpret, since the salt is scarcely dissociated under these conditions if measurements of conductance can be taken as a guide.

This investigation was initiated by Professor E. D. Hughes, F.R.S., and Professor C. K. Ingold, F.R.S., and we are indebted to them and to Mr. C. A. Vernon for many discussions. Technical assistance by Mr. T. J. Collins and Mr. E. Grayson is greatly appreciated.

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Preparation and Polymerisation of Some 3 : 3-Disubstituted Oxacyclobutanes.

By A. C. Farthing.

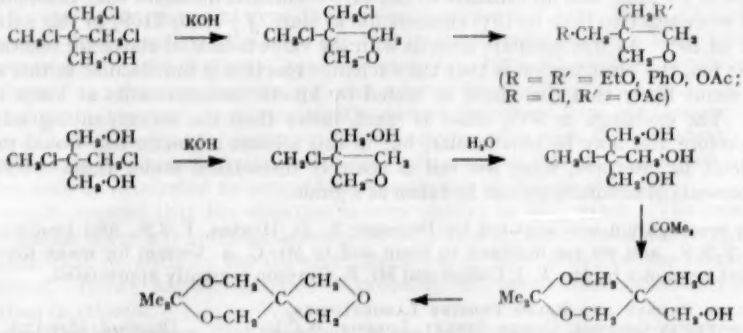
[Reprint Order No. 6428.]

The preparation of some 3 : 3-disubstituted oxa*cyclo*butanes, mainly derived from pentaerythritol, and an improved preparation of pentaerythritol monochloride are described. The oxa*cyclo*butanes are polymerised by powerful electrophilic catalysts to yield linear polyethers. The properties of the polymers are correlated with the nature of the substituent group. Solution polymerisation below room temperature gives the highest molecular weights. The boron trifluoride-catalysed polymerisation of 3 : 3-bischloromethyloxa*cyclo*butane does not proceed in the absence of water : admission of traces of water results immediately in polymerisation.

The preparation of a number of substituted oxa*cyclo*butanes, in particular some derived from pentaerythritol, was undertaken as a preliminary to a study of their polymerisation (a preliminary communication to the XIII International Congress of Pure and Applied Chemistry was published in *J. Polymer Sci.*, 1954, **12**, 503). The literature on oxa*cyclo*butanes from pentaerythritol has been reviewed by Marrian (*Chem. Rev.*, 1948, **43**, 149).

Oxa*cyclo*butanes are made by the dehydrohalogenation of the appropriate 1 : 3-halogenohydrins. Because of the unfavourable steric factors, oxa*cyclo*butane itself can be obtained in this way only in very poor yield (Derrick and Bissell, *J. Amer. Chem. Soc.*, 1916, **38**, 2478), though by treatment of the acetate of the chlorohydrin with solid potassium hydroxide Searles (*ibid.*, 1951, **73**, 124) was able to improve the yield to 45%. We have obtained 3 : 3-dimethyloxa*cyclo*butane from the chlorohydrin in only 19% yield. When the central carbon atom bears two more bulky substituents the reacting groups are brought closer together, and good yields of the oxa*cyclo*butanes are obtained. Thus Govaert and Beyaert (*Natuurw. Tijdschr.*, 1940, **22**, 73), obtained 3 : 3-bischloromethyloxa*cyclo*butane in 70—80% yield from pentaerythritol trichloride, and using substantially their conditions we have obtained it in high yield.

We have now carried out the annexed syntheses from pentaerythritol di- and trichloride, prepared as described by Mooradien and Cloke (*J. Amer. Chem. Soc.*, 1945, **67**, 942).



Replacement of the chlorine atoms in 3 : 3-bischloromethyloxa*cyclo*butane by other groups required very vigorous conditions, as might be expected from the *neo*pentyl-type structure of the compound. The preparations of pentaerythritol monochloride and of 3 : 3-bisacetoxymethyloxa*cyclo*butane are more convenient than those hitherto reported.

It is well known that boron trifluoride and other powerful electrophilic compounds polymerise many ethenoid compounds and also some strained three- and five-membered heterocycles. The mechanism is undoubtedly ionic and has been widely investigated in

recent years (for a review see Hamann, *Angew. Chem.*, 1951, **63**, 231). The polymerisation of oxa*cyclo*butanes to polyethers has, however, not hitherto been studied. The work now reported is the subject of B.P. 723,777.

$$\begin{matrix} CR_2{-}CH_2 \\ CH_2{-}O \end{matrix} \longrightarrow [-O{\cdot}CH_2{\cdot}CR_2{\cdot}CH_2-]_n$$

Linear polyethers have been made by extension of the classical methods for ether preparation; but such reactions rarely proceed quantitatively and the molecular weight of the polymer is accordingly limited. Thus, heating glycols with acid catalysts does give polyethers, but if the terminal hydroxyl group is lost by olefin formation the growth of the macromolecule ceases. This method has succeeded in the case of 2 : 3 : 5 : 6-tetramethyl-*p*-xylylene glycol (Rhoad and Flory, *J. Amer. Chem. Soc.*, 1950, **72**, 2216) where the peculiar structure of the glycol does not allow side-reactions. The Williamson reaction, using dihalides and disodium derivatives of glycols, has also been used to make polyethers (U.S.P. 2,060,715). The polymerisation of cyclic ethers is more attractive because the moiety which would require to be eliminated in a condensation reaction (water or sodium halide) is removed before the polymerisation. This can prove an advantage on purely manipulative grounds. In polymerisation of ethylene oxide (see Hamann, *loc. cit.*, for references) the molecular weight of the product is again limited by side-reactions, including isomerisation to acetaldehyde. As a general method the ring opening of cyclic ethers is of course limited by the stability of the ring.

However, for oxa*cyclo*butanes we have found that the polymerisation can proceed to high molecular weight. Thus in the case of 3 : 3-bischloromethyloxa*cyclo*butane, the monomer principally studied, it has been possible to polymerise to such molecular weight that the polymer could be spun to fibres which exhibit the property of " cold-drawing."

The polymerisation is very exothermic and consequently difficult to control when monomer alone is used. Thus conditions of bulk polymerisation were not suitable for a detailed study of the reaction. However, this method affords a rapid way of making polymers on a small scale in order that some structure–property relations may be established. The following Table summarises results so far obtained.

*Structure–property relations in oxa*cyclo*butane polymers, viz.,* $\left[-O{\cdot}CH_2{\cdot}\overset{\displaystyle CH_2R}{\underset{\displaystyle CH_2R'}{C}}{-}CH_2-\right]_n$.

R	R′	M. p.		Solubility in H_2O
Cl	Cl	180°	Cryst.	Insol.
Cl	OAc	72	Amorphous	Insol.
OAc	OAc	—	Amorphous	Sol.
OH	OH	>280	Cryst.	Insol.
Me	Me	47	Cryst.	Insol.
OEt	OEt	75—83	Cryst.	Insol.
OPh	OPh	85	Amorphous	Insol.

The polymer where R = R′ = OH could not be made directly. It was prepared by polymerising 7 : 7-dimethyl-2 : 6 : 8-trioxa*spiro*[3 : 5]nonane, which gave an amorphous polymer freely soluble in benzene. The protecting ketal group was removed by hydrolysis to yield a range of polymers. As the hydroxyl groups were freed the polymer became insoluble in non-polar solvents and soluble only in highly polar solvents, and after acid hydrolysis at 100° it became insoluble even in highly polar solvents such as formic acid. This change in properties is due probably to progressively increasing hydrogen-bonding between the polymer chains, and may be compared to that in analogous derivatives of cellulose. Attempts to prepare linear polymers from oxa*cyclo*butanes containing free hydroxyl groups resulted in cross-linked polymers, as would be expected.

The properties of the other polymers in the Table are governed by the symmetry, polarity, and size of the substituent groups and may be correlated with these factors.

The polymerisation of 3 : 3-bischloromethyloxa*cyclo*butane has been studied in more detail. The molecular weights of the polymers from 3 : 3-bischloromethyloxa*cyclo*butane were compared by melt-viscosity measurements. An absolute measure of molecular weight has not yet been made because solution-viscosity measurements were anomalous, probably

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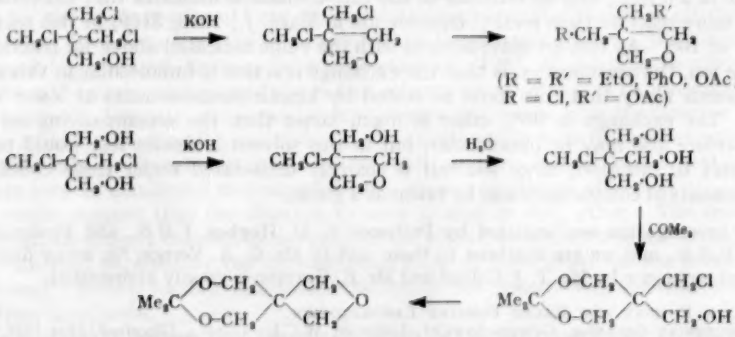
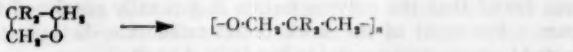
We have now carried out the annexed syntheses from pentaerythritol di- and trichloride, prepared as described by Mooradien and Cloke (*J. Amer. Chem. Soc.*, 1945, **67**, 942).



Replacement of the chlorine atoms in 3 : 3-bischloromethyloxa*cyclo*butane by other groups required very vigorous conditions, as might be expected from the *neo*pentyl-type structure of the compound. The preparations of pentaerythritol monochloride and of 3 : 3-bisacetoxymethyloxa*cyclo*butane are more convenient than those hitherto reported.

It is well known that boron trifluoride and other powerful electrophilic compounds polymerise many ethenoid compounds and also some strained three- and five-membered heterocycles. The mechanism is undoubtedly ionic and has been widely investigated in

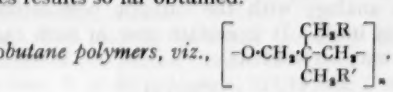
recent years (for a review see Hamann, *Angew. Chem.*, 1951, **63**, 231). The polymerisation of oxa*cyclo*butanes to polyethers has, however, not hitherto been studied. The work now reported is the subject of B.P. 723,777.



Linear polyethers have been made by extension of the classical methods for ether preparation; but such reactions rarely proceed quantitatively and the molecular weight of the polymer is accordingly limited. Thus, heating glycols with acid catalysts does give polyethers, but if the terminal hydroxyl group is lost by olefin formation the growth of the macromolecule ceases. This method has succeeded in the case of 2 : 3 : 5 : 6-tetramethyl-*p*-xylylene glycol (Rhoad and Flory, *J. Amer. Chem. Soc.*, 1950, **72**, 2216) where the peculiar structure of the glycol does not allow side-reactions. The Williamson reaction, using dihalides and disodium derivatives of glycols, has also been used to make polyethers (U.S.P. 2,060,715). The polymerisation of cyclic ethers is more attractive because the moiety which would require to be eliminated in a condensation reaction (water or sodium halide) is removed before the polymerisation. This can prove an advantage on purely manipulative grounds. In polymerisation of ethylene oxide (see Hamann, *loc. cit.*, for references) the molecular weight of the product is again limited by side-reactions, including isomerisation to acetaldehyde. As a general method the ring opening of cyclic ethers is of course limited by the stability of the ring.

However, for oxa*cyclo*butanes we have found that the polymerisation can proceed to high molecular weight. Thus in the case of 3 : 3-bischloromethyloxa*cyclo*butane, the monomer principally studied, it has been possible to such molecular weight that the polymer could be spun to fibres which exhibit the property of " cold-drawing."

The polymerisation is very exothermic and consequently difficult to control when monomer alone is used. Thus conditions of bulk polymerisation were not suitable for a detailed study of the reaction. However, this method affords a rapid way of making polymers on a small scale in order that some structure–property relations may be established. The following Table summarises results so far obtained.

Structure–property relations in oxacyclobutane polymers, viz.,  .

R	R′	M. p.		Solubility in H_2O
Cl	Cl	180°	Cryst.	Insol.
Cl	OAc	72	Amorphous	Insol.
OAc	OAc	—	Amorphous	Sol.
OH	OH	>280	Cryst.	Insol.
Me	Me	47	Cryst.	Insol.
OEt	OEt	75—83	Cryst.	Insol.
OPh	OPh	85	Amorphous	Insol.

The polymer where R = R′ = OH could not be made directly. It was prepared by polymerising 7 : 7-dimethyl-2 : 6 : 8-trioxa*spiro*[3 : 5]nonane, which gave an amorphous polymer freely soluble in benzene. The protecting ketal group was removed by hydrolysis to yield a range of polymers. As the hydroxyl groups were freed the polymer became insoluble in non-polar solvents and soluble only in highly polar solvents, and after acid hydrolysis at 100° it became insoluble even in highly polar solvents such as formic acid. This change in properties is due probably to progressively increasing hydrogen-bonding between the polymer chains, and may be compared to that in analogous derivatives of cellulose. Attempts to prepare linear polymers from oxa*cyclo*butanes containing free hydroxyl groups resulted in cross-linked polymers, as would be expected.

The properties of the other polymers in the Table are governed by the symmetry, polarity, and size of the substituent groups and may be correlated with these factors.

The polymerisation of 3 : 3-bischloromethyloxa*cyclo*butane has been studied in more detail. The molecular weights of the polymers from 3 : 3-bischloromethyloxa*cyclo*butane were compared by melt-viscosity measurements. An absolute measure of molecular weight has not yet been made because solution-viscosity measurements were anomalous, probably

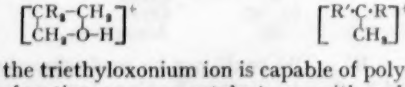
because the high intra- and inter-molecular forces do not allow the molecules of dissolved polymer to separate and open out completely. This explanation is consistent with the high crystallinity and low solubility of the polymer at room temperature.

It was found that the polymerisation is generally catalysed by powerful electrophilic substances. For most of the work boron trifluoride–diethyl ether complex (BF_3,Et_2O) was selected because it was easier to handle and purify.

Bulk polymerisation did not give really high molecular weights, probably owing to lack of temperature control and consequent decomposition of the "gegenion." Accordingly polymerisation in solution, under reflux, was examined. Solvents boiling above room temperature gave lower molecular weights than did bulk polymerisation. The use of lower-boiling solvents such as methyl chloride gave much higher molecular weights. Thus bulk polymerisation yielded polymer of melt viscosity ~200 poises at 197°, polymerisation in methyl chloride ~200 poises at 277°. In all the work attention was paid to the conditions of dryness of the reagents and apparatus, with the precautions commonly used for water-sensitive organic reactions. However, about 30 experiments revealed that experimental results (yield and viscosity of polymer) could not be accurately reproduced, nor could these results be correlated with any of the experimental conditions. It was apparent that some critical factor had not been brought under control. In view of the work of A. G. Evans (see, *e.g.*, Hamann, *loc. cit.*) on the importance of co-catalysis in *iso*butene polymerisation it appeared likely that co-catalytic effects were responsible for this lack of reproducibility, and suspicion was directed to variable traces of water (cf. Norris and Russell, *Trans. Faraday Soc.*, 1952, **48**, 91). An apparatus was accordingly devised in which the polymerisation could be carried out in the presence of controlled, minute amounts of water. It was then shown unequivocally that a co-catalyst is necessary for reaction. Under rigorously dry conditions, reaction did not take place until admission of traces (of the order of 0·01%) of water. The influence of the proportion of co-catalyst has not yet been determined accurately, but when the proportion of water was kept to such a low level it was possible to make polymer of considerably higher molecular weight than hitherto.

An analogy with the cationic polymerisation of ethenoid compounds immediately suggests itself. It is certain now in both cases that the monomer–"catalyst" adduct, which may be written:

is not capable of inducing polymerisation. On admission of water protons are generated, which initiate polymerisation through oxonium or carbonium ions:



It has been shown that the triethyloxonium ion is capable of polymerising oxa*cyclo*butanes.

Whether ether can function as a co-catalyst, as with polymerisation of *iso*butene (Evans and Meadows, *J. Polymer Sci.*, 1949, **4**, 359), has not yet been established. When the boron trifluoride–ether complex was used, as described above, traces of water would certainly also be present.

Experimental

3 : 3-*Bischloromethyloxa*cyclo*butane*.—Potassium hydroxide (70% K_2O; 435 g., 1 mol.) was dissolved in 98% ethanol (2½ l.). Then were added pentaerythritol trichloride (1240 g., 1 mol.) and also trichloride (285 g.) recovered from a previous preparation, slightly contaminated with the oxa*cyclo*butane. The solution was boiled under reflux, with stirring, for 15 min., and left to cool. Potassium chloride (483 g.) was filtered off and washed with ethanol. The combined liquors were concentrated, filtered, and fractionated, to yield 3 : 3-bischloromethyloxa*cyclo*butane (925 g.), b. p. 80°/10 mm., and trichloride (370 g.), b. p. 130°/12 mm. containing a little oxa*cyclo*butane. With allowance for recovered trichloride the yield was ~90%. The 3 : 3-bischloromethyloxa*cyclo*butane, purified by drying (CaH_2), followed by distillation at 0·05 mm., had m. p. 18·7°, d_{25}^{25} 1·2951, n^{20} 1·4858.

3 : 3-*Bisacetoxymethyl-* and 3-*Acetoxymethyl-*3-*chloromethyl-oxa*cyclo*butane*.—3 : 3-Bischloromethyloxa*cyclo*butane did not react with potassium acetate in boiling ethanol or acetic acid. Consequently it was heated alone with anhydrous potassium acetate (2 mols.) for 4 hr. at 180°. The product was filtered and washed with dry ether. After removal of the ether the residue was fractionally distilled, to yield two main fractions, b. p. 42—44°/0·05 mm. and 68°/0·05 mm. The former, when redistilled (b. p. 120—121°/13 mm.; 30% yield) was 3-*acetoxymethyl*-3-*chloromethyloxa*cyclo*butane* (Found: C, 46·7; H, 5·7; Cl, 18·65. $C_7H_{11}O_3Cl$ requires C, 47·0; H, 6·15; Cl, 18·9%). The second fraction, b. p. 152°/21 mm. (60% yield), was 3 : 3-bisacetoxymethyloxa*cyclo*butane (Found: C, 52·9; H, 7·0. Calc. for $C_9H_{14}O_5$: C, 52·4; H, 6·9%) as described by Govaert and Bayaert (*Proc. Acad. Sci. Amsterdam*, 1939, **42**, 790).

3-*Chloromethyl*-3-*hydroxymethyloxa*cyclo*butane*.—Pentaerythritol dichloride (1015 g.) in ethanol (700 c.c.) was stirred in a 5-l. flask under reflux, with gentle heating to dissolve the dichloride. Potassium hydroxide (325 g.; 1 mol.) in ethanol (1·3 l.) was then added during 5 min., with stirring. Next morning the solution was boiled for 5 min. Potassium chloride was filtered off and washed with ethanol. The liquors were concentrated and the residue fractionated, to yield a syrup, b. p. 120—130°/10 mm. (585 g.), and a mixture of syrup and crystals, b. p. 130—148°/10 mm. (139 g.). The latter fraction was largely unchanged starting material; the former (86% yield) was redistilled at 64°/0·09 mm. and was 3-*chloromethyl*-3-*hydroxymethyloxa*cyclo*butane* (Found: C, 43·5; H, 6·6; Cl, 26·0. $C_5H_9O_2Cl$ requires C, 44·0; H, 6·6; Cl, 26·2%).

Pentaerythritol Monochloride.—3-Chloromethyl-3-hydroxymethyloxa*cyclo*butane (400 g.) in water (2 l.) containing concentrated sulphuric acid (3·0 c.c.) was boiled under reflux for 6 hr. After partial concentration the acid was precipitated with barium hydroxide and removed by filtration. After total removal of the water the residue was distilled, to give pentaerythritol chloride, b. p. 160°/0·09 mm. (368 g.; 81%).

5-*Chloromethyl*-5-*hydroxymethyl*-2 : 2-*dimethyl*-1 : 3-*dioxan*.—The preceding product was dissolved in pure acetone (2 l.) containing dry hydrogen chloride (20 g.). The solution was left overnight and then stirred with excess of anhydrous potassium carbonate until neutral. After removal of acetone the residue was distilled, to yield 374 g. (80%) of 5-*chloromethyl*-5-*hydroxymethyl*-2 : 2-*dimethyl*-1 : 3-*dioxan*, b. p. 80°/0·1 mm. (Found: C, 49·6; H, 7·6; Cl, 18·7. $C_8H_{15}O_3Cl$ requires C, 49·4; H, 7·7; Cl, 18·3%). A sample with 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid gave acetone 2 : 4-dinitrophenylhydrazone.

7 : 7-*Dimethyl*-2 : 6 : 8-*trioxa*spiro[3 : 5]*nonane*.—The chloride from the preceding preparation was dehydrochlorinated in the same manner as the pentaerythritol chlorides, to yield 66% of 7 : 7-*dimethyl*-2 : 6 : 8-*trioxa*spiro[3 : 5]*nonane*, b. p. 40°/0·15 mm., 91°/13 mm. (Found: C, 60·8; H, 8·7. $C_8H_{14}O_3$ requires C, 60·75; H, 8·85%).

3 : 3-*Bisphenoxymethyloxa*cyclo*butane* [Prepared by Mr. J. M. Phillipson].—3 : 3-Bischloromethyloxa*cyclo*butane was heated with dry potassium phenoxide (2 mols.) at 120—125° for 2 hr. and the mixture directly distilled, to yield 40% of 3 : 3-*bisphenoxymethyloxa*cyclo*butane*, b. p. 143°/0·05 mm., m. p. 68° (from methanol) (Found: C, 75·6; H, 6·6. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·6%).

3 : 3-*Bisethoxymethyloxa*cyclo*butane* [Prepared by Dr. P. C. Johnson].—3 : 3-Bischloromethyloxa*cyclo*butane (31·0 g.) was added to a solution of potassium (25·0 g.) in dry ethanol (150 c.c.). The solution was boiled under reflux for 20 hr. and when cold filtered from potassium chloride. Ethanol was removed, finally at the water pump. The distillate was fractionated, to give 3 : 3-*bisethoxymethyloxa*cyclo*butane*, b. p. 81·5—82°/19 mm. (23 g., 68%) (Found: C, 62·2; H, 9·9. $C_9H_{18}O_3$ requires C, 62·0; H, 10·3%).

3-*Chloro*-2 : 2-*dimethylpropan*-1-*ol*.—2 : 2-Dimethylpropan-1 : 3-diol was treated with 1 mol. each of pyridine and thionyl chloride under the conditions used by Mooradien and Cloke (*loc. cit.*) for pentaerythritol. The mixture was taken up in water (1 l.) and acidified with concentrated hydrochloric acid, then extracted three times with ether; the extract was dried ($MgSO_4$) and the ether removed. The residue was fractionated, to yield the chloride, b. p. 78—80°/10 mm. (240 g., 54%).

3 : 3-*Dimethyloxa*cyclo*butane*.—The preceding chlorohydrin (248 g.) was slowly added to potassium hydroxide (250 g.) with stirring, at such a rate that the temperature of the distillate did not exceed 80°. When reaction ceased the remaining volatile matter was distilled off at room temperature to a condenser at −70° by application of water-pump vacuum. The total condensate was dried with potassium hydroxide and fractionated, to yield 3 : 3-dimethyloxa*cyclo*butane, b. p. 79·5—80° (33 g., 19%) (cf. Bennett and Phillip, *J.*, 1928, 1937).

Polymer from 3 : 3-*Bischloromethyloxa*cyclo*butane*.—The molecular weights of the various

preparations of the polymer were compared by measurement of melt viscosity, which is given in poises at the temperature of measurement. There being no solvent available which dissolved the polymer at 25°, the following solution viscosities were determined at 100° and 0·5 g./100 c.c. in *o*-dichlorobenzene:

Logarithmic viscosity no.	18·0	23·8	19·0	16·0
Melt viscosity at 197°	390	150	25	210

On one polymer sample the following results were obtained:

Logarithmic viscosity no.	27·0	23·8	18·6	23·2
Concn. (g./100 c.c.)	0·25	0·5	1·0	2·0

Another sample of logarithmic viscosity no. 16·0 at 0·5% was capable of forming oriented fibres, whereas all the samples above were of too low a molecular weight to be cold-drawn.

Bulk polymerisations. Portions of 3:3-bischloromethyloxa*cyclo*butane (60 g.) were treated with boron trifluoride–diethyl ether complex (redistilled; 0·15 c.c. and 0·3 c.c.). After 3 min. and 1 min. respectively the two mixtures became very hot and viscous. On being kept overnight the polymers became opaque. Each was heated at 197°/15 mm. for 50 min.; 21·3% and 20·8% respectively of monomer was thus removed, leaving polymer of melt viscosity 390 and 150 at 197°.

Solution polymerisation above room temperature. Monomer (10 c.c.) in pure dry solvent (10 c.c.) was treated with boron trifluoride–diethyl ether (redistilled; 2·0 c.c.). After *ca.* 2 min. the solution was boiled under reflux for *ca.* 30 sec. and set to a pale pink paste. The solid polymer was filtered off, washed with dry ether, and dried at 100°, to give the following results:

Solvent	Yield (g.)	η (at 197°)	Softening point
Methylene dichloride	12	24	178°
Benzene	9	26	180
Ether	11	24	178

Many other solvents were examined, of b. p. above room temperature, with various monomer and catalyst concentrations, but the viscosity of the products remained at 20—60 at 197°.

Solution polymerisation below room temperature. A flask fitted with (i) a cold-finger type of reflux condenser carrying a calcium chloride tube, (ii) a stirrer, sealed with rubber tubing, and (iii) an aperture for addition of reagents, was assembled hot from components dried at 100° for at least 1 hr. The condenser was charged with solid carbon dioxide and ethanol, and a known volume of solvent distilled in from the cylinder, through several drying towers of sodium hydroxide or calcium chloride. The flask was cooled and a known volume of monomer added, followed by boron trifluoride–diethyl ether. The reaction was left to proceed at the temperature of reflux. A wide range of conditions was covered, solvents being methyl chloride, sulphur dioxide, and dichlorofluoromethane. Monomer concentration varied from 50 to 30% and catalyst proportion from 1·5 to 5% (on monomer). The melt viscosities obtained were from 60 to 240 at 277°, much higher than those obtained above room temperature; but the results were not reproducible nor could the influence of experimental conditions be discerned.

Properties of the polymer. The polymer was a tough solid, softening point 180° (penetrometer method, Edgar and Ellery, *J.*, 1952, 2633). It was highly crystalline. Fibres could be spun from the molten polymer and these could readily be cold-drawn to yield highly oriented specimens of identity period 4·8 Å (calc. 4·92 Å for the fully extended repeating unit). It had very high *X*-ray absorption, no doubt due to the high chlorine content (Found: Cl, 45·35. Calc. for $[C_5H_8OCl_2]_n$: Cl, 45·6%). It was insoluble generally at room temperature, but freely soluble at 100° in chlorinated hydrocarbons, esters, and amines.

Polymers from 3-*Chloromethyl*-3-*hydroxymethyl- and* 3:3-*Bishydroxymethyl-oxa*cyclo*butane, and* 2:6-*Dioxa*spiro[3:3]*heptane.*—Each of these compounds rapidly polymerised with traces of boron trifluoride–diethyl ether. Polymer was formed round the drop of catalyst and often stopped further reaction. The polymers were insoluble and infusible without decomposition. The last two monomers were made by recorded methods (Marrian, *Chem Rev.*, 1948, **43**, 149).

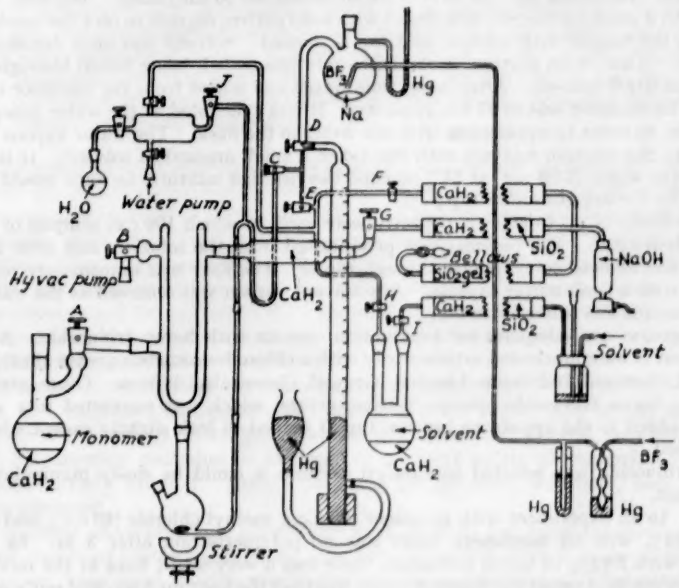
Polymer from 3:3-*Bisacetoxymethyloxa*cyclo*butane.*—The monomer (5 g.) with boron trifluoride–diethyl ether (0·05 c.c.) reacted slowly compared with the bischloromethyl derivative. The temperature of the mixture did not rise above 35°. On storage overnight there was left a soft colourless and clear resin, hygroscopic, and freely soluble in hot and cold water.

Polymer from 3-*Acetoxymethyl*-3-*chloromethyloxa*cyclo*butane.*—The monomer (25 g.) was treated with boron trifluoride–diethyl ether (0·3 c.c.). Overnight the mixture became a hard brittle resin, softening point (copper block) 72°, insoluble in water.

Polymer from 3:3-*Dimethyloxa*cyclo*butane.*—The monomer was extremely sensitive to

boron trifluoride–diethyl ether. Thus monomer (2 c.c.) and catalyst (0·05 c.c.) reacted immediately with evolution of heat. Polymerisation occurred immediately at −70° with the same mixture. In all cases the viscous polymer set to a white wax, m. p. 47° (capillary), giving a sharply defined *X*-ray diffraction pattern. It was insoluble in water and ethanol, soluble in benzene.

Polymer from 7 : 7-*Dimethyl*-2 : 6 : 8-*trioxa*spiro[3 : 5]*nonane and its Conversion into* lin.-*Polypentaerythritol.*—The spiran (20 g.) was treated with boron trifluoride–diethyl ether (0·2 c.c.). Overnight the mixture set to a tough translucent solid, m. p. 102° (capillary), soluble in benzene. The polymer was cut into flakes and immersed in water for 2 days. The flakes became brittle and the water contained acetone (identified as 2 : 4-dinitrophenylhydrazone). The flakes were ground in a mortar and covered with N-hydrochloric acid for 1 hr. The polymer was collected, washed with water, and dried over sodium hydroxide. It then had m. p. 220—250°, and was insoluble in benzene and soluble in *m*-cresol to give a viscous solution. Further treatment



with 0·2N-hydrochloric acid at 100° for 1·5 hr. gave a polymer, m. p. >280°, insoluble in formic acid, *m*-cresol, and cupriethylenediamine reagent, and giving an *X*-ray photograph characteristic of a crystalline compound. Treatment of the above *m*-cresol solutions with traces of concentrated hydrochloric acid resulted in immediate gelation. Infrared analysis of the polymers showed the formation of hydrogen-bonded hydroxyl groups as hydrolysis proceeded.

Polymer from 3 : 3-*Bisethoxymethyloxa*cyclo*butane.*—Boron trifluoride–diethyl ether (0·1 c.c.) was added to monomer (1 c.c.) in boiling methyl chloride (1 c.c.). After the solution had boiled under reflux for 5 hr. methanol (1 c.c.) was added. The mixture was diluted with ether, and the polymer filtered off and dried [0·5 g.; m. p. 75—83° (capillary), softening at ~45°]. *X*-Ray examination showed it to be highly crystalline. It was insoluble in water.

Polymer from 3 : 3-*Bisphenoxymethyloxa*cyclo*butane.*—Boron trifluoride–diethyl ether (0·05 c.c.) was added to a solution of monomer (1·0 g.) in dichlorofluoromethane (1 c.c.). After the solution had boiled under reflux for 3 hr. methanol (1 c.c.) was added and the polymer isolated by decantation and dried. It was a clear glassy resin, m. p. ~85° (capillary).

Other Catalysts in Oxacyclobutane Polymerisations.—Bentonite, trifluoroacetic acid, and tris-2-chloroethyl borate were without effect. Boron trifluoride–acetic acid complex (BF_3,2AcOH) and triethyloxonium fluoroborate were active catalysts, stannic chloride was less active, and concentrated sulphuric acid least active, on the basis of qualitative test-tube experiments with various monomers.

"Dry" Apparatus.—The apparatus is reproduced, roughly to scale except for the long drying tubes, in the Figure. The central part, bounded by taps *A*, *B*, *C*, *D*, *E*, *G*, and *J* could

be evacuated to 0·02 mm. and then heated to ~200° to remove water and other volatile materials. Other parts were kept dry by calcium hydride. Monomer and solvent were dried over calcium hydride, and boron trifluoride over flakes of sodium. Exits from the apparatus were protected by tubes 3 ft. long and 1½ in. in diameter packed with silica gel and calcium hydride. These long tubes were themselves protected from the atmosphere. The condenser and its attached calcium hydride tube up to tap *G* were wound with " Nichrome " wire connected to a 25-v transformer for heating the glass. The rest of the apparatus was heated with a free flame. The reaction mixture was stirred magnetically.

The use of the apparatus may largely be inferred from inspection of the Figure. Solvent was distilled into the solvent reservoir at least 24 hr. before use and stored there over calcium hydride. Monomer, already dried by calcium hydride, was added to the monomer reservoir as required and kept at least 24 hr. over calcium hydride before use. The apparatus was dried by heating and evacuation and left to cool whilst connected to the pump. Monomer was then distilled up to a mark on the reaction vessel with solid carbon dioxide to cool the condenser, the vacuum was discharged with solvent, and tap *G* opened. Solvent was next distilled up to a second mark. Then, with stirring, boron trifluoride was added, being forced through the tube by use of the hand bellows. After some time water was added from the chamber to initiate reaction. The chamber was of 97 c.c. capacity. It was evacuated at the water pump and left for *ca.* 30 min. to come to equilibrium with the water in the flask. The water vapour was then transferred to the reaction mixture with the aid of a small amount of solvent. It is doubtful whether all the water (2·26 mg. at 25°) reached the reaction mixture, as some would probably be adsorbed by the dry glass after tap *J*.

Reaction flasks of up to 500 c.c. capacity were used, in which 100 c.c. samples of monomer could be polymerised. The polymer was precipitated from the solution, and after 2—3 days the solvent was allowed to evaporate through tap *G*. The flask was immediately replaced by a fresh one, with a fresh stirrer capsule. Any solvent vapour was removed at the water pump, and the apparatus was ready for re-use.

Silicone grease was adequate for taps not in contact with boron trifluoride. After trial, taps *C*, *D*, and *E* were lubricated satisfactorily with a chlorofluorocarbon grease kindly supplied by Imperial Chemical Industries Limited, General Chemicals Division. Other greases were degraded by boron trifluoride (except Silicone grease, which was converted into a cement) Tap *C* was added to the apparatus because tap *D* tended to leak slightly except when it was freshly greased.

Boron trifluoride was selected as catalyst because it could be easily manipulated under dry conditions.

Results. In an experiment with monomer (20 c.c.), methyl chloride (60 c.c.), and boron trifluoride (1·93% w/w on monomer), there was no polymerisation after 3 hr. In a similar experiment with 3·92% of boron trifluoride there was a very slight haze in the mixture after 22 min. The reaction vessel was lowered by the length of the joint for 5 sec. and replaced. There was an immediate precipitate of white clots of polymer. To monomer 10 c.c., methyl chloride (20 c.c.), and boron trifluoride (90 c.c.) (at 21°/765 mm.; 0·252 g., 1·95% on monomer) there was added the contents of the water-vapour chamber (97 c.c. of water vapour at 21°/18·6 mm.; 1·77 mg.). There was an immediate precipitate of polymer. After 22 hours' reaction the reaction flask was detached and some methanol added. There were recovered 13 g. of polymer (100% yield).

The melt viscosities of the polymer obtained varied between 300 and 3000 poises at 277°.

In a higher-boiling solvent, dichlorofluoromethane (b. p. +8·9°; cf. methyl chloride −24·22°), and similar amounts of reagents, melt viscosities of 200—300 poises at 277° were obtained. However, these figures were obtained during early experiments with the apparatus and the lower viscosities may be a consequence of a somewhat higher adventitious moisture content.

The author thanks Dr. H. Gudgeon for advice and encouragement, Mr. A. M. Jones for valuable experimental assistance throughout the whole of the work, Dr. C. J. Brown for *X*-ray measurements, and Mr. J. S. F. Gill for melt-viscosity determinations.

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The Salting-out of Non-electrolytes. Part III. The Inert Gases and Sulphur Hexafluoride.*

By T. J. Morrison and N. B. B. Johnstone.

[Reprint Order No. 6317.]

The salting-out of helium, krypton, and sulphur hexafluoride has been studied, electrolytes varying over a wide range of ionic size being used. Neon, argon, xenon, oxygen, *n*-butane, and benzene have also been investigated in solutions of electrolytes of special interest. Neither purely electrostatic theories of the effect nor the "internal pressure" theory of McDevit and Long is generally valid. Comparison of solutes of approximately the same size, *e.g.*, sulphur hexafluoride and benzene, suggests that the polarisability of the solute molecule is at least as important as solute volume in determining the salting-out effect especially with large ions. For the smaller ions there is a good correlation between salting-out and the entropy change in solution of the non-electrolyte in pure water at 4°.

It has been shown that certain electrolytes give salting-out coefficients for the paraffin gases and other non-polar solutes which are approximately linear functions of the coefficients for sodium chloride (Parts I and II *). The slopes of these lines were not in general in agreement with the values predicted from purely electrostatic theories of the effect. McDevit and Long (*J. Amer. Chem. Soc.*, 1952, **74**, 1773), using benzene as solute, reached essentially similar conclusions as to the salting-out order of electrolytes, and suggested that the effect might be related to the volume change which occurs when liquid electrolyte is dissolved in water, or to the closely related "effective pressure" of the electrolyte derived from compressibility measurements.

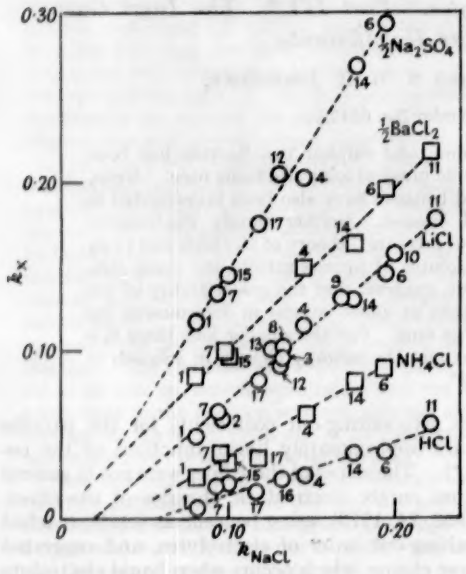
The present investigation has been mainly concerned with the salting-out of helium, krypton, and sulphur hexafluoride, but work on neon, argon, and xenon showed that a more extended study of these gases would not affect the general conclusions reached. Sulphur hexafluoride provides an example of an inert solute of somewhat different type from those already studied. Additional data for benzene, *n*-butane, and oxygen have also been obtained.

The method of comparison previously used (Part I) has been retained, and k_x for a given salt has been plotted against k_{NaCl} at 25°. The fact that k_x is an additive function has, however, been used to give results for cations as chlorides and for anions as sodium salts. It is found that, while a number of ions give, for all the non-polar solutes so far studied, reasonably linear relation (Fig. 1), yet the remaining ions do not. In some cases (Fig. 2) the inert gases and sulphur hexafluoride show approximately normal behaviour but other solutes deviate beyond experimental error in the direction of greater salting-in. With the ions NMe_4^+ and NEt_4^+, even helium, krypton, and sulphur hexafluoride show appreciable deviations from linear behaviour, while *n*-butane and benzene are highly salted-in (Fig. 3). For salts of this type, giving a very large expansion on solution, the salting-out coefficients referred to unit volume of solution (k_v) and to unit weight of water (k_w) differ appreciably, so that although k_w indicates slight salting-in for helium and krypton, k_v would indicate salting-out of the same magnitude as for ammonium chloride. Since k_w appears to be more closely related to theoretically significant concentration units (mole-fraction) it has been retained in the present paper.

The slopes of the lines for the inert gases and sulphur hexafluoride are compared in Table 1 with those predicted (*a*) from electrostatic theories of the type suggested by Debye and McAulay (*Physikal. Z.*, 1925, **26**, 22) and (*b*) from McDevit and Long's internal-pressure theory. Although the observed slopes for the substituted ammonium salts are of necessity very approximate, they must certainly be regarded as positive, and the internal-pressure theory fails when tested in these cases on the most inert solutes available. Neither

* Parts I and II, *J.*, 1952, 3814, 3819.

FIG. 1.



Key to all Figures.

1. He	10. C_2H_6
2. Ne	11. C_4H_{10}
3. A	12. C_3H_4
4. Kr	13. N_2
5. Xe	14. C_6H_6
6. SF_6	15. C_2H_2
7. H_2	16. O_2
8. CH_4	17. N_2O
9. C_3H_8	

1—13. This series, Parts I, II, III. Additional data for 7, 12, 13 from Seidell (" Solubilities of Inorganic and Organic Substances," van Nostrand, N.Y.).

14. McDevit and Long (*loc. cit.*) and this paper.

15, 17. Seidell (*op. cit.*).

16. Seidell (*op. cit.*) and this paper.

FIG. 2.

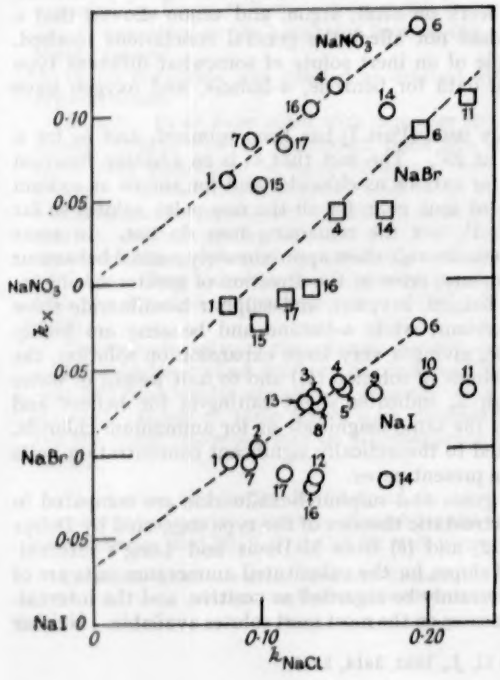
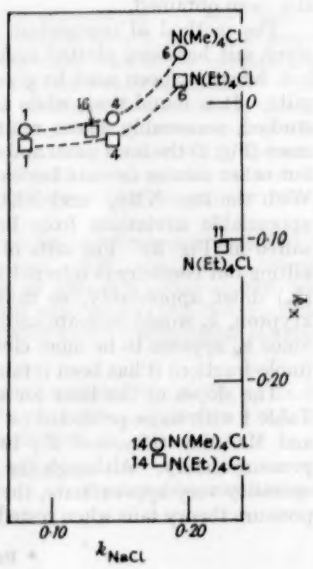


FIG. 3.



theory can, in fact, be regarded as satisfactory, although, apart from the cases mentioned, McDevit and Long's theory does reproduce better the order in which electrolytes salt out.

The most striking feature of these comparisons is the increasing deviation from inert-gas behaviour of benzene with increase in ionic size. It is clear from comparison with sulphur hexafluoride, which is probably of the same order of size as benzene, that no theory which utilises molecular volume as the only or the main solute parameter controlling salt effects can be qualitatively satisfactory, even if allowance is made, as suggested by McDevit and Long, for the finite size of solute molecules and ions. Thus neither purely electrostatic theories, which have been shown to involve solute volume as the main solute characteristic for non-polar molecules (Cohn and Edsall, " Proteins, Amino Acids and Peptides," Reinhold, N.Y.), nor the internal-pressure theory using molecular volume as the only solute parameter, is *generally* valid.

It has been suggested by several workers that van der Waals forces between ions and

FIG. 4.

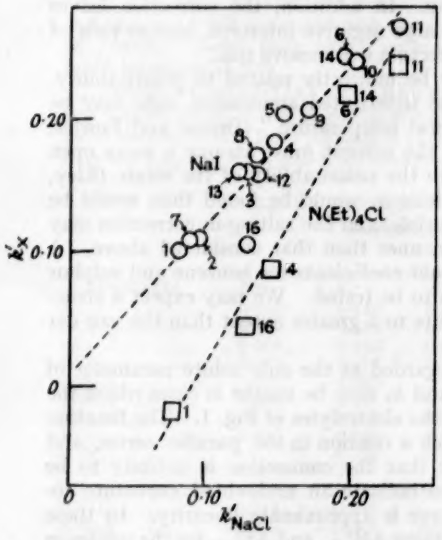
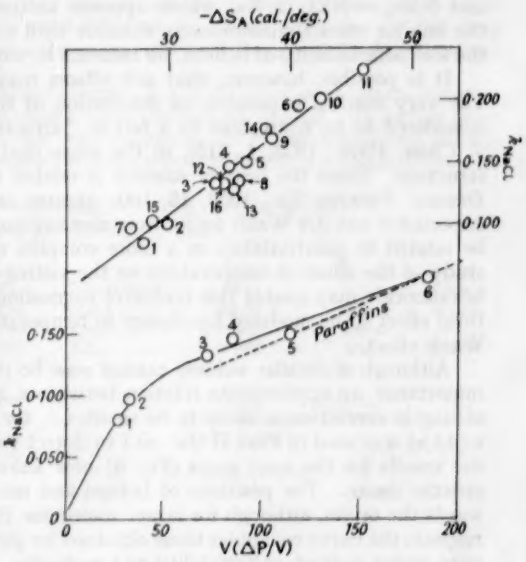


FIG. 5.



neutral molecules may be in part responsible for the specific effects observed in this field, and it is noteworthy that benzene and sulphur hexafluoride differ rather considerably in polarisability for substances of nearly the same molecular volume. It is therefore of interest to determine whether differences in polarisability would account empirically for

TABLE 1.

Electrolyte	obs.	Slope calc. *a*	*b*	Electrolyte	obs.	Slope calc. *a*	*b*	Electrolyte	obs.	Slope calc. *a*	*b*
HCl ...	0·33	—	0·21	$\frac{1}{2}BaCl_2$...	0·96	1·2	1·19	NaI	0·70	0·95	0·64
LiCl ...	0·87	1·14	0·74	NMe_4Cl	0·4	0·75	−1·1	$NaNO_3$	0·77	—	0·74
KCl ...	0·83	0·90	0·81	NEt_4Cl	0·4	0·7	negative	$\frac{1}{2}Na_2SO_4$	1·50	1·28	1·58
NH_4Cl...	0·58	0·87	0·36	NaBr ...	0·91	0·98	0·83				

the deviations from linear behaviour noted above. If, for example, we assume that the difference between k_{NaI} for the two solutes ($\Delta k = 0{\cdot}104$) is due entirely to difference in polarisability ($\Delta p_g = 6{\cdot}3 \times 10^{-24}$), a correction for salting-in, varying directly with polarisability, can be applied to all the solutes investigated. A similar, though much

smaller, correction is necessary for sodium chloride and the corrected coefficients, k'_x, are plotted in Fig. 4. It is evident that the correction is quantitatively sufficient to account for the deviations of the paraffin series and ethylene. For the substituted ammonium salts the correction is nearly three times that for sodium iodide and the resulting plot for tetraethylammonium chloride (Fig. 4) is again reasonably linear, although we have as yet much fewer data than for the iodide. The position of oxygen, which is salted-in by iodide ions relative to chloride, is little changed when the correction is applied, and it is likely that in this case at least there is a specific interaction. In view of the chemical nature of the particles concerned, however, this is not surprising. With tetraethylammonium chloride, on the other hand, there is no such effect and oxygen shows approximately inert-gas behaviour.

Although these results suggest that polarisability is a factor of major importance in controlling salt effects, there are indications that the problem cannot be dealt with as simply as we have outlined. Thus the true order of salting-out, apart from that due to van der Waals forces, estimated from the slopes of the corrected lines would be $I > Br > Cl$ and $NMe_4 = NEt_4 > Na$, which appears unlikely. In addition, the correction leaves the line for tetraethylammonium chloride with a large negative intercept, and in view of the low polarisability of helium, no reasonable correction will remove this.

It is possible, however, that salt effects may be indirectly related to polarisability. The very marked expansion on dissolution of the substituted ammonium salts may be considered to be equivalent to a fall in "structural temperature" (Bernal and Fowler, *J. Chem. Phys.*, **1933**, **1**, 515), in the sense that the solvent must assume a more open structure. Since the heat of solution is related to the polarisability of the solute (Eley, *Discuss. Faraday Soc.*, **1953**, **15**, 150), greater salting-in would be found than would be expected if van der Waals forces were alone responsible, and the salting-in correction may be related to polarisability in a more complex manner than that considered above. A study of the effect of temperature on the salting-out coefficients for benzene and sulphur hexafluoride may enable this tentative suggestion to be tested. We may expect a structural effect to be modified by change in temperature to a greater extent than the van der Waals effect.

Although molecular volume cannot now be regarded as the only solute parameter of importance, an approximate relation between v_c and k_x may be sought in cases where the salting-in correction is likely to be small, *i.e.*, for the electrolytes of Fig. 1. The function $v_c(\Delta p/v)$ was used in Part II (*loc. cit.*) to detect such a relation in the paraffin series, and the results for the inert gases (Fig. 5) now show that the connection is unlikely to be strictly linear. The positions of helium and neon indicate an undoubted curvature towards the origin, although for larger molecules there is approximate linearity. In these respects the curve resembles those obtained by plotting ΔH°_{277} and ΔS°_{277} for the solutes in pure water against polarisability and molecular volume respectively (Morrison and Johnstone, *J.*, **1954**, **3441**). There is a good correlation between ΔS°_{277} and k_{NaCl} (Fig. 5) for all the non-polar solutes; that involving ΔH°_{277} is less satisfactory. The other electrolytes of this group will give similar relations, and these suggest that the problem of the primary salting-out effect requires more knowledge of the structure of the solvent round the inert molecule and how it is affected by the presence of ions than is at present available.

Experimental

The solubility technique has been described (Morrison and Billett, *J.*, **1952**, **3819**), and the inert gases were the purest obtainable from the British Oxygen Co. Ltd. Sulphur hexafluoride (at least 99% pure) was supplied by Imperial Chemical Industries Limited. As was predicted (Morrison and Johnstone, *loc. cit.*) the solubility of this gas, though slightly higher than that of carbon tetrafluoride, is very low, and the salting-out coefficients are therefore somewhat less accurate than for the more soluble gases. Errors of up to about $\pm 0{\cdot}010$ in k_x would not, however, affect the conclusions reached at the present stage of the investigation, and this margin is certainly not exceeded. Solubilities are recorded in Table 3 for a short temperature range, and from these a value for ΔS°_{277} of 40·8 cal. per degree (for transfer of gas at 1 atm. to a hypothetical solution at unit mole-fraction) was calculated.

The salting-out of benzene was determined in a few cases by measuring the solubility of air saturated with benzene vapour at 25° in an apparatus similar to that used for other gases. From the known vapour pressure of benzene and the solubility of air at 1 atm., the solubility of benzene can be obtained. This method is being developed for measuring the solubilities of volatile liquids for which analytical methods are difficult and, although air is a suitable carrier gas for benzene (making a contribution to the solubility of the mixture of only about 15 c.c. in 500 c.c.), in other cases one of the more sparingly soluble gases, such as carbon tetrafluoride, would be more satisfactory. Although the solubility of benzene by this method (1·64 g. per l. at 25°) is slightly less than that recorded by McDevit and Long (*loc. cit.*; 1·77 g. per l.) the salting-out coefficients for KCl, KI, and NMe_4I were in good agreement with the results of these workers. A determination using NEt_4Br left no doubt that very marked salting-in occurs with salts of this type.

In most cases concentrations of the electrolytes were approximately N, and were controlled by volumetric and density methods. For NMe_4I, however, the low solubility limits the concentration to about 0·25N at 25°.

Previous values of k_x for helium and argon at high salt concentrations by Akerlof (*J. Amer. Chem. Soc.*, 1935, **57**, 1196) are generally in poor agreement with our results, especially for argon (*e.g.*, $k_{NaCl} = 0·058$ compared with our value of 0·133), but the results of Eucken and Herzberg (*Z. physikal. Chem.*, 1950, **195**, 1) on argon and xenon agree well ($k_{NaCl} = 0·139$ for argon and 0·150 for xenon at 20°).

Results are recorded in Table 2 for a sufficient number of salts in the cases of helium, krypton, and sulphur hexafluoride to enable the additivity rule to be directly applied. In certain other cases the conversion from potassium to sodium salts was carried out by using the linear relation between k_{KCl} and k_{NaCl} which appears to apply generally to a sufficient degree of accuracy.

TABLE 2. *Salting-out coefficients,* $k = (\log s_0/s)/c$, *at 25°. Concentrations per 1000 g. of water.*

	k				k		
Electrolyte	He	Kr	SF_6	Electrolyte	Ne	Ar	Xe
NaCl	0·081	0·146	0·195	NaCl	0·097	0·133	0·149
LiCl	0·050	0·116	0·145	LiCl	0·059	0·096	—
HCl	0·008	0·028	0·040	KI	0·080	0·108	0·113
KCl	0·068	0·124	0·165			k	
NH_4Cl	0·027	0·065	0·090		C_2H_6	n-C_4H_{10}	O_2
$\frac{1}{2}BaCl_2$	0·086	0·151	0·195	KCl	0·145 (0·148)	—	—
$\frac{1}{2}Na_2SO_4$	0·118	0·203	0·295	KI	0·049 (0·042)	—	—
KI	0·083	0·120	0·145	KBr	—	0·174	—
KBr	—	0·120	0·160	NMe_4I	−0·333 (−0·336)	—	—
NaBr	0·087	—	—	NEt_4Br	−0·295	−0·122	−0·046
KNO_3	—	0·093	0·120				
HNO_3	−0·013	−0·003	—				
NMe_4I	−0·001	−0·016	0·010				
NEt_4Br	−0·024	−0·032	0·010				

Values in parentheses have been calculated from the data given by McDevit and Long (*loc. cit.*).

TABLE 3. *Solubility of sulphur hexafluoride (c.c. at N.T.P. per 1000 g. of water at a gas pressure of 1 atm.)*

t	10·9°	12·5°	14·2°	19·6°	25·0°	27·8°	29·6°
s_0	7·9	7·4	7·0	6·2	5·4	5·2	5·1

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Sugar Nitrates. Part II. The Preparation and Reactions of Some Nitrates, Sulphonates, Sulphinates, and other Esters of Methyl* 4 : 6-O-*Benzylidene-α-*D*-glucoside.*

By JOHN HONEYMAN and J. W. W. MORGAN.

[Reprint Order No. 6435.]

Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate and other D-glucoside 2 : 3-dinitrates with sodium iodide in acetone or methanol, or with sodium nitrite in aqueous ethanol, give the 3-nitrates. Evidence is given suggesting that the course of the reaction with sodium iodide is:

$$>CH\cdot O\cdot NO_2 \xrightarrow{NaI} >CH\cdot ONa \xrightarrow{MeOH} >CH\cdot OH$$

The de-esterification of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate, 2 : 3-dimethanesulphonate, 2 : 3-dinitrate, 3-nitrate 2-toluene-*p*-sulphonate, and 2-nitrate 3-toluene-*p*-sulphonate with sodium methoxide at 0°, or at room temperature, proceeds by initial removal of the group on $C_{(3)}$. In the hydrolysis of the nitrates, inorganic nitrite is produced and the products are not isolated quantitatively; the 2 : 3-dinitrate gives an α-diketone identified as its quinoxaline derivative. The migration of a nitrate group from $C_{(3)}$ to $C_{(2)}$ is noted.

When the 2 : 3-dinitrate, 3-nitrate, and 3-nitrate 2-toluene-*p*-sulphonate are de-esterified by sodium methoxide in boiling methanol the 2 : 3-anhydro-α-D-alloside and α-D-glucoside, and the 3-nitrate are obtained. The 2-nitrate 3-toluene-*p*-sulphonate gives the anhydro-α-D-alloside only. Except for the 3-nitrate, yields are low.

When heated with sodium benzenesulphinate in acetic anhydride methyl 4 : 6-*O*-benzylidene-α-D-glucoside and its 2 : 3-diacetate both give the 2 : 3-dibenzenesulphinate, which yields the parent D-glucoside when de-esterified by sodium methoxide. The 2 : 3-sulphite and 2 : 3-dichloroacetate are similarly de-esterified.

NITRATE esters of carbohydrates have been prepared by the slow addition of freshly mixed fuming nitric acid and acetic anhydride (Honeyman and Morgan, *Chem. and Ind.*, 1953, 1035) to a solution or suspension of the sugar derivative in acetic anhydride at 0°. Not only were ethylidene and benzylidene groups not removed during esterification, but the aromatic ring in the benzylidene compounds was not nitrated, making methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate readily available.

Reaction of the 2 : 3-dinitrate with sodium iodide in acetone at 100° is the standard method for preparing methyl 4 : 6-*O*-ethylidene-β-D-glucoside 3-nitrate (Bell and Synge, *J.*, 1938, 833). During the present work methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate was conveniently converted into the 3-nitrate by sodium iodide in boiling acetone or methanol, or best by sodium nitrite in boiling aqueous ethanol. The corresponding ditoluene-*p*-sulphonate, dimethanesulphonate, and diacetate were all recovered unchanged when heated with sodium iodide in acetone for 20 hours at 100°. A possible mechanism, suggested in Part I, for removal of a secondary nitrate group by sodium iodide is:

$$>CH\cdot O\cdot NO_2 + NaI \longrightarrow >CHI + NaNO_3$$
$$>CHI + H_2O \longrightarrow >CH\cdot OH + HI$$

The water required in the second stage was presumed to react when the product was being washed with water. This mechanism, which does not account for the invariable production of free iodine and nitric oxide during these reactions, requires that the aqueous extracts of the reaction mixture should be acidic, whereas they were always neutral. Moreover,

* Part I, *J.*, 1952, 2778. A summary was presented at the New York meeting of the American Chemical Society, September, 1954.

similar iodo-compounds are stable to alcohol and to water (Newth, Richards, and Wiggins, *J.*, 1950, 2356).

In view of these discrepancies, and the presence of inorganic nitrite in the products, the following alternative mechanism is suggested :

$$\text{>CH·O·NO}_2 + \text{NaI} \longrightarrow \text{>CH·ONa} + \text{NO}_2\text{I}$$
$$\text{NO}_2\text{I} + \text{NaI} \longrightarrow \text{NaNO}_2 + \text{I}_2$$

When acetone was the solvent the products included pungent, lachrymatory iodine-containing acetone derivatives, probably produced in this way :

$$3\text{>CH·ONa} + 3\text{I}_2 + \text{COMe}_2 \longrightarrow 3\text{>CH·OH} + \text{CI}_3\text{·COMe} + 3\text{NaI}$$

These side reactions make acetone unsuitable for quantitative investigation of the reaction and, indeed, the perfect solvent was not found. Finally methanol was used; although it does not undergo the iodoform reaction, it is partly oxidised to formaldehyde. The proposed reaction sequence is :

$$2\text{>CH·O·NO}_2 + 2\text{NaI} \longrightarrow \text{>2CH·ONa} + 2\text{NO}_2\text{I}$$
$$2\text{>CH·ONa} + 2\text{MeOH} \longrightarrow \text{>2CH·OH} + 2\text{NaOMe}$$
$$2\text{NO}_2\text{I} + 2\text{NaI} \longrightarrow 2\text{NaNO}_2 + 2\text{I}_2$$
$$\text{I}_2 + 2\text{NaOMe} \longrightarrow \text{CH}_2\text{O} + 2\text{NaI} + \text{MeOH}$$

i.e., combining these :

$$2\text{>CH·O·NO}_2 + 2\text{NaI} + \text{MeOH} \longrightarrow 2\text{>CH·OH} + 2\text{NaNO}_2 + \text{I}_2 + \text{CH}_2\text{O}$$

In this scheme each nitrate group yields one sodium nitrite molecule and one iodine atom. The liberated iodine was first estimated by titration against sodium thiosulphate solution. The mixture was then shaken with chloroform and water, the organic products passing into the chloroform. The nitrite present in the aqueous layer was estimated under nitrogen. The results in Table 1 were obtained with methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate (2 g.); the balance of organic compounds is incomplete.

TABLE 1.

	Organic products			Inorganic products	
		3-Nitrate			
Reaction time (hr.)	Unchanged (%)	%	mole	Iodine (g.-atom)	Nitrite (mole)
3	51	27	0·00144	0·00166	0·00130
3	—	—	—	0·0020	0·0020
6	29	43	0·00232	0·00237	0·00167
6	—	—	—	0·0037	0·0034
18	0	60	0·00324	0·00143	0·00128

As far as the inorganic compounds were concerned, the results were not reproducible and reliable quantitative information was not obtained. The course of the reactions leading to the by-products is more complex than represented, and other factors, not yet understood, are involved. Prolonged heating leads to loss of free iodine although the reactions were carried out in sealed tubes; a slow reaction is proceeding in which iodine is consumed with simultaneous loss of nitrite. This, together with the evolution of nitric oxide, may be due to :

$$3\text{NaNO}_2 + \text{MeOH} + \text{I}_2 \longrightarrow \text{NaNO}_3 + 2\text{NaI} + 2\text{NO} + \text{CH}_2\text{O}$$

Evidence that on $C_{(2)}$ and $C_{(3)}$ one nitrate group activates the other was obtained when the esters of methyl 4 : 6-*O*-benzylidene-α-D-glucoside shown in Table 2 were subjected to the action of sodium iodide in acetone at 100° for 20 hours. Additional results are summarized in Table 3, where, unless stated, the compounds are esters of methyl 4 : 6-*O*-benzylidene-α-D-glucoside. These results indicate that attachment to $C_{(2)}$ of a sulphonate group assists removal of the nitrate on $C_{(3)}$, and that even an acetate group on $C_{(2)}$ has a slight activating effect. The stability of the ditoluene-*p*-sulphonate and the dimethanesulphonate is

explained by the strong deactivation produced on one group by the electron-attracting effect of the other (Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 821).

No study has been made of the course of removal of a nitrate group by sodium nitrite but the appearance of the reaction and especially the absence of brown fumes suggests a different mechanism.

TABLE 2.

Reactant	Product	
3-Nitrate	Unchanged	(66%)
	Methyl 4 : 6-*O*-benzylidene-α-D-glucoside	(21%)
3-Nitrate 2-toluene-*p*-sulphonate	2-Toluene-*p*-sulphonate	(66%)
2-Methanesulphonate 3-nitrate	2-Methanesulphonate	(73%)
2-Acetate 3-nitrate	Unchanged	(34%)
	Mixture of the 2- and the 3-acetate	(46%)

TABLE 3.

Compound	Reaction conditions	Product
2 : 3-Diacetate	NaI, acetone, 20 hr., ST	Unchanged, 95%
2 : 3-Ditoluene-*p*-sulphonate	NaI, acetone, 21 hr., ST	Unchanged, 88%
2 : 3-Dimethanesulphonate	NaI, acetone, 20 hr., ST	Unchanged, 83%
2 : 3-Dinitrate	NaI, acetone, 20 hr., R	Unchanged, 13% 3-Nitrate, 47%
	Acetone alone, 17 hr., R	Unchanged, 93%
	$NaNO_2$, aq. ethanol, 21 hr., R	3-Nitrate, 70% Glucoside, 5%
Methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-dinitrate	NaI, acetone, 24 hr., ST	3-Nitrate
	NaI, pyridine, 30 min., R	3-Nitrate, 54%
	Pyridine, 30 min., 100°	Unchanged, 77%
Methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate	NaI, pyridine, 17 hr., R	Unchanged, 65%

R = reflux; ST = sealed tube at 100°; glucoside = methyl 4 : 6-*O*-benzylidene-α-D-glucoside.

The results in Part I show that nitrate groups are removed by alkyl–oxygen or nitryl–oxygen fission; from methyl 4 : 6-*O*-alkylidene-D-glucoside 2 : 3-dinitrates the corresponding D-glucoside and 2 : 3-anhydro-D-alloside are obtained. The same conclusion has been reached by Anbar, Dostrovsky, Samuel, and Yoffe (*J.*, 1954, 3603) who studied the hydrolysis of alkyl mononitrates by the use of ^{18}O. Sodium methoxide in methanol–chloroform at 0°, or at room temperature, or in boiling dry methanol was used for the de-esterifications now to be described. Mild alkaline hydrolysis of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate for 3 days at 0°, or for 5 days at room temperature, gave a small amount of starting compound, the corresponding 3-nitrate (about 25%), and, under the latter conditions, the 2-nitrate (6%). Extensive decomposition occurred when the hydrolysis mixture was boiled for one hour and only minute amounts of methyl 4 : 6-*O*-benzylidene-α-D-glucoside, its 3-nitrate, and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside were obtained. Pure recrystallized methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate, similarly treated for 7 days at room temperature, yielded starting compound (44%) and methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate (5%). This is the first recorded instance of the migration of a nitrate group. When the hydrolysis mixture containing the 3-nitrate was boiled for an hour, methyl 4 : 6-*O*-benzylidene-α-D-glucoside (35%) and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (21%) resulted. Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate was less stable than its 2-methyl ether to alkali; under the same conditions 11% and 66% respectively of each was recovered. These yields are much lower than those reported in Part I, but the earlier results could not be substantiated. Hydrolysis of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate 2-toluene-*p*-sulphonate at 0° gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate (36%), unchanged starting compound (11%), and 2-nitrate (1%): again some migration of the nitrate group from $C_{(3)}$ to $C_{(2)}$ occurred. When the hydrolysis mixture was boiled for an hour, methyl 4 : 6-*O*-benzylidene-α-D-glucoside (10%) and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (8%) were obtained. Part I included the report that methyl 4 : 6-*O*-propylidene-α-D-glucoside 3-nitrate 2-toluene-*p*-sulphonate was converted, by 24

hours' boiling with sodium methoxide in methanol, almost quantitatively into the anhydro-α-D-alloside. Again this was repeated and found to be false. After 1 hour's boiling, the hydrolysis mixture contained starting compound (10%), 3-nitrate (12%), and a trace of impure anhydro-α-D-alloside. Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate 3-toluene-*p*-sulphonate hydrolysed at 0° gave methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (32%), methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-toluene-*p*-sulphonate (9%), and starting compound (13%), but when reaction was conducted by boiling under reflux the anhydro-α-D-alloside and a trace of an unidentified crystalline solid were the only products isolated. Despite some discrepancies in detail, these results confirm the general conclusions reached in Part I that nitrate esters can be cleaved by alkali both by nitryl–oxygen and alkyl–oxygen fission, but emphasize that yields are often low.

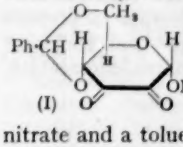
The percentage yields of the products obtained in the de-esterifications are summarized in Table 4. Although reaction conditions for all the hydrolyses were not identical, certain general conclusions can be drawn.

TABLE 4. *Alkaline hydrolysis of esters of methyl* 4 : 6-O-*benzylidene-*α*-*D*-glucoside (yields, %).*

Group on $C_{(3)}$:	$O{\cdot}NO_2$		OH		$O{\cdot}SO_2{\cdot}C_7H_7$		$O{\cdot}NO_2$	
Group on $C_{(2)}$:	$O{\cdot}NO_2$		$O{\cdot}NO_2$		$O{\cdot}NO_2$		$O{\cdot}SO_2{\cdot}C_7H_7$	
Products	A	B	A	B	A	B	A	B
Unchanged	16	0	0	0	11	0	13	0
3-Nitrate	21	2	44	11	36	3	0	0
2-Nitrate	6	0	5	0	1	0	0	0
Glucoside	0	2	0	35	0	10	0	0
Anhydro-D-alloside	0	3·5	0	21	0	8	32	21
3-Toluene-*p*-sulphonate	0	0	0	0	0	0	9	0
Total	43	7·5	49	67	48	21	54	21

A = hydrolysis at room temperature or 0°. B = hydrolysis in boiling solvent.
Glucoside = methyl 4 : 6-*O*-benzylidene-α-D-glucoside.

The first three compounds in Table 4, *i.e.*, the dinitrate, 3-nitrate, and 3-nitrate 2-toluene-*p*-sulphonate, each reacted with sodium methoxide at or below room temperature, to give mainly the 3-nitrate, but in contrast with the same reactions carried out in boiling solvent no methyl 4 : 6-*O*-benzylidene-α-D-glucoside nor methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside was isolated. The low overall yields in the other de-esterifications also suggested that another reaction was proceeding, and the presence of much nitrite indicated that this is the reaction in which ketone and nitrite are produced. This was confirmed by the isolation of the quinoxaline derivative of the α-diketone, methyl 4 : 6-*O*-benzylidene-2 : 3-dideoxy-2 : 3-dioxo-α-D-glucoside (I), when the de-esterification of the dinitrate was effected in the presence of *o*-phenylene diamine. The products obtained on hydrolysis in boiling solvent show that with the 3-nitrate 63% of reacted compound was accounted for by reactions leading to methyl 4 : 6-*O*-benzylidene-α-D-glucoside and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside. When the substituents were a nitrate and a toluene-*p*-sulphonate group, the amount of these products was less, whereas with the dinitrate mere traces of them were isolated. All these reactions in boiling methanol were accompanied by rapid darkening and the production of nitrite, indicating that here also and particularly with the dinitrate, the other reaction was taking place, the ketonic products being decomposed in boiling alkali. Contrasting with these results was the conversion of methyl α-D-glucoside 2 : 3 : 4-triacetate 6-nitrate into methyl 3 : 6-anhydro-α-D-glucoside in high yield, with negligible ketone formation. This confirms Gladding and Purves's results (*J. Amer. Chem Soc.*, 1944, **66**, 76) and shows that in the removal of this nitrate group from a primary carbon atom, alkyl–oxygen fission is the major, if not the only, course of hydrolysis.


(I)

Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate reacts when heated for several hours with pyridine at 100° to give an unidentified syrup unless hydroxylamine hydrochloride was included in the reaction mixture, in which case a small amount of the dioxime of the diketone (I) was isolated.

The almost quantitative conversion of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate into the 2 : 3-anhydro-D-alloside by sodium methoxide in methanol and chloroform (Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727) illustrates a general property of sulphonates. The course of this hydrolysis, and that of the corresponding dimethanesulphonate, has now been clarified. The first step, removal of the group on $C_{(2)}$ by sulphonyl–oxygen fission without inversion, occurs readily. Mild treatment of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dimethanesulphonate with sodium methoxide gave the corresponding 3-methanesulphonate (40%) and unchanged compound (25%) : longer reaction gave the 2 : 3-anhydro-α-D-alloside (66%) and 3-methanesulphonate (10%). With the ditoluene-*p*-sulphonate extended reaction time leads to the 2 : 3-anhydro-α-D-alloside only (Richtmyer and Hudson, *loc. cit.*), but shorter treatment yielded the 2 : 3-anhydro-α-D-alloside (36%) and the 3-toluene-*p*-sulphonate (18%).

By heating methyl 4 : 6-*O*-benzylidene-α-D-glucoside with sodium benzenesulphinate in acetic anhydride at 100° a reaction ensued which was complete in 18 hours but not after 3 hours; a by-product was precipitated in 30 minutes. If, however, the corresponding 2 : 3-diacetate was used, a precipitate was formed at once, and the reaction was complete in 30 minutes. This suggests that acetylation is first necessary and then the acetate is replaced by sulphinate. Aromatic sulphoxides were not obtained when benzene or anisole was treated with the same reagent, in contrast to the preparation of aromatic sulphones from sulphonic acids and trifluoracetic anhydride (Bourne, Stacey, Tatlow, and Tedder, *J.*, 1951, 718) but phenyl benzenethiolsulphonate was precipitated on pouring each of these reaction solutions into water and also that obtained when only sodium benzenesulphinate and acetic anhydride were heated together. Sodium methoxide in methanol–chloroform converted the 2 : 3-dibenzenesulphinate into methyl 4 : 6-*O*-benzylidene-α-D-glucoside (about 80%), *i.e.*, the sulphinate behaves in this reaction like a carboxylic ester, as was also found by Balfe, Kenyon, and Tarnoky (*J.*, 1943, 446).

When sodium toluene-*p*-sulphonate, sodium sulphite, and benzoic acid were each heated separately with methyl 4 : 6-*O*-benzylidene-α-D-glucoside in acetic anhydride, the only sugar derivative isolated was the 2 : 3-diacetate.

Under controlled conditions, the action of thionyl chloride in pyridine on methyl 4 : 6-*O*-benzylidene-α-D-glucoside has now given a crystalline 2 : 3-sulphite, which was converted into the parent glucoside derivative by sodium methoxide. The sulphite was very sensitive to acid; it decomposed on ordinary storage and was converted quantitatively into methyl α-D-glucoside by a trace of acid in aqueous acetone, showing that the sulphite group renders the benzylidene group unusually labile.

The 2 : 3-dichloroacetates of methyl 4 : 6-*O*-ethylidene- and 4 : 6-*O*-benzylidene-α-D-glucoside were readily prepared from chloroacetic anhydride and sodium chloroacetate, and were reconverted into the glucoside by sodium methoxide. Attempts to prepare similar diesters of methyl 4 : 6-*O*-ethylidene-α-D-glucoside by dichloro- and trichloroacetyl chloride in pyridine led only to the monodichloroacetate and monotrichloroacetate, in low yields.

Experimental

Unless otherwise stated, chloroform solutions were dried over sodium sulphate before being evaporated, evaporations were carried out under reduced pressure, and the light petroleum used had b. p. 60—80°.

Chromatographic separations were carried out with columns of activated alumina, Type H, 100/200 S mesh, supplied by Messrs. Peter Spence and Sons, Ltd.

At the end of the reaction time specified for the preparation of esters in pyridine a little water was added to decompose excess of acid chloride. After a further 15 min. the mixture was poured into ice-water, and the resulting syrup was repeatedly washed with water until it solidified. Nitrates were isolated by pouring the reaction mixture into aqueous potassium carbonate and washing the precipitate repeatedly with water until it crystallized. Exceptional cases are fully described below.

The presence of nitrite was established by the appearance of a red colour after the addition of a solution of sulphanilic acid in acetic acid, followed by a solution of α-naphthylamine.

Identifications were by mixed m. p.

Preparation of Methyl 4 : 6-O-*Ethylidene*-α-D-*glucoside*.—(*a*) Methyl α-D-glucoside (20 g.), paraldehyde (200 ml.), and concentrated sulphuric acid (20 drops) were shaken at room temperature for 1 hr. Solid potassium carbonate was then added to the solution, which had been diluted with chloroform; the whole was filtered, and the filtrate was evaporated, leaving a syrup, which solidified when shaken with water. The solid (4·7 g.), recrystallized from ethanol–acetone, was methyl 4 : 6-*O*-ethylidene-2 : 3-*O*-oxydiethylidene-α-D-glucoside, m. p. 181—182°. The aqueous solution was evaporated to a syrup which was extracted several times with hot ether. The combined ethereal extracts yielded, on concentration, methyl 4 : 6-*O*-ethylidene-α-D-glucoside (11·5 g.), m. p. 75—76°. These yields varied somewhat in different experiments.

(*b*) Methyl 4 : 6-*O*-ethylidene-2 : 3-*O*-oxydiethylidene-α-D-glucoside (2 g.) was shaken with acetone (100 ml.), until almost all the solid had dissolved, and then N-hydrochloric acid (1 ml.) was added. The solution was left at room temperature for several hours, and then neutralized with potassium carbonate. The filtrate was evaporated to a residue which was triturated with water. Undissolved starting compound (0·53 g.) was collected and the aqueous filtrate was evaporated to a solid which was boiled with ether. On concentration and cooling of the ether extract, methyl 4 : 6-*O*-ethylidene-α-D-glucoside (0·76 g.) was obtained.

Preparation of Nitrates with Nitric Acid in Acetic Anhydride.—(1) *Methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2 : 3-*dinitrate*. Fuming nitric acid (2 ml.) in acetic anhydride (5 ml.) was added slowly to a solution of methyl 4 : 6-*O*-ethylidene-α-D-glucoside (2 g.) in acetic anhydride (5 ml.) at 0°. The mixture was allowed to warm to room temperature during 15 min., and then solid potassium carbonate was added. The solid (2·75 g.) obtained by pouring the mixture into ice-water was recrystallized from light petroleum, giving methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-dinitrate, m. p. 101°, $[\alpha]_D^{18}$ +140·5° (*c*, 1·0 in $CHCl_3$).

(2) *Methyl* 4 : 6-O-*ethylidene*-β-D-*glucoside* 2 : 3-*dinitrate*. Fuming nitric acid (6·4 ml.) in acetic anhydride (20 ml.) was added to a suspension of methyl 4 : 6-*O*-ethylidene-β-D-glucoside (7·4 g.) in acetic anhydride (20 ml.) at 0°, and the mixture was kept at 0° for 1 hr. with occasional shaking. The crude solid (9·27 g., 89%) recrystallized from light petroleum or methanol as stout needles of methyl 4 : 6-*O*-ethylidene-β-D-glucoside 2 : 3-dinitrate (7·69 g.), m. p. 88—89°, $[\alpha]_D^{21}$ −21·3° (*c*, 1·0 in $CHCl_3$).

Methyl 4 : 6-*O*-ethylidene-β-D-glucoside (2·2 g.) was added to a solution of chloroform (10 ml.), acetic anhydride (1·5 ml.), and fuming nitric acid (1·9 ml.) at 0°. The solution was allowed to warm to room temperature in 5 min., and then shaken with aqueous potassium carbonate. The chloroform layer was evaporated to a syrup, which gave a solid (1·1 g., 35%) when stirred under water. Recrystallization from light petroleum yielded the dinitrate, m. p. 88—89°. With reaction times of 15 min. and 1 hr., the yields were 32% and 29% respectively.

(3) *Methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*dinitrate*. Ice-cold fuming nitric acid (8 ml.) in acetic anhydride (20 ml.) was added slowly to methyl 4 : 6-*O*-benzylidene-α-D-glucoside (10 g.) suspended in acetic anhydride (20 ml.) at 0°. The product obtained after 15 min. at 0° gave, after recrystallizing from methanol or light petroleum, prisms of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*dinitrate* (8·3 g.), m. p. 124—125°, $[\alpha]_D^{19}$ +87·8° (*c*, 1·1 in $CHCl_3$) (Found : C, 45·0; H, 4·2. $C_{14}H_{16}O_{10}N_2$ requires C, 45·2; H, 4·3%).

Conversion of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Dinitrate into the* 4 : 6-O-*Ethylidene Analogue*.—Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate (1 g.) in paraldehyde (10 ml.) containing concentrated sulphuric acid (2 drops) was shaken for 30 min. at room temperature. The solution was neutralized with solid potassium carbonate and filtered, and the filtrate was evaporated to a syrup, which solidified when stirred with water. Two recrystallizations of the solid (0·75 g.) from light petroleum gave needles of methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-dinitrate, m. p. 100—101°.

Preparation of Esters of Methyl 4 : 6-O-*Ethylidene*-α-D-*glucoside*.—(1) 2 : 3-*Diacetate*. Methyl 4 : 6-*O*-ethylidene-α-D-glucoside (5 g.) and sodium acetate (1·5 g.) in acetic anhydride (15 ml.) were heated at 100° for 1 hr. Pouring the mixture into ice-water and adding solid potassium carbonate precipitated an oil, which solidified on stirring. This product (5·95 g.), recrystallized from light petroleum, was *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2 : 3-*diacetate*, m. p. 81°, $[\alpha]_D^{16}$ +117° (*c*, 1·0 in $CHCl_3$) (Found : C, 51·9; H, 6·8; OMe, 9·9. $C_{13}H_{20}O_8$ requires C, 51·3; H, 6·6; OMe, 10·2%).

(2) 2 : 3-*Ditoluene*-p-*sulphonate*. Toluene-*p*-sulphonyl chloride (5·7 g.) in pyridine (10 ml.) was added to the glucoside (2·2 g.) in pyridine (10 ml.) and the solution kept for 3 days at room temperature. The solid product (4·3 g.), recrystallized from ethanol, gave methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate, m. p. 155°, $[\alpha]_D^{19}$ +50·9° (*c*, 1·2 in $CHCl_3$).

(3) 2 : 3-*Dichloroacetate*. The glucoside (10 g.), chloroacetic anhydride (30 g.), and sodium chloroacetate (3 g.) were heated at 100° for 1 hr., then poured into a concentrated, iced solution of potassium carbonate. After several changes of water a solid was obtained, a methanolic solution of which was decolorized with charcoal, concentrated, and cooled to 0°. The resulting fine needles (12 g.), recrystallized from aqueous methanol, yielded stout needles of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2 : 3-*dichloroacetate*, m. p. 75—76°, $[\alpha]_D^{21}$ +104° (*c*, 1·1 in $CHCl_3$) (Found : C, 41·4; H, 4·8. $C_{13}H_{16}O_8Cl_2$ requires C, 41·8; H, 4·8%). The fine needles when kept at room temperature melted and changed into the other form. If the stout needles were cooled in methanol at 0° and seeded with the fine form, complete conversion into the fine form was observed.

(4) *Monodichloroacetate*. Dichloroacetyl chloride (10 ml.) in pyridine (10 ml.) at 0° was added slowly to the glucoside (5 g.) in pyridine (10 ml.), cooled in ice. When the initial reaction had subsided, the mixture was kept at room temperature for 24 hr., before being poured into ice-water. The syrup which separated was dissolved in chloroform, and washed with 10% hydrochloric acid, sodium hydrogen carbonate solution, and water. Evaporation gave a solid, which recrystallized from methanol, as *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside monodichloroacetate* (0·2 g.), m. p. 201° (Found : C, 40·3; H, 4·5. $C_{11}H_{16}O_7Cl_2$ requires C, 39·9; H, 4·8%).

(5) *Monotrichloroacetate*. Trichloroacetyl chloride (11 g.) was added slowly to the glucoside (4·4 g.) in pyridine (20 ml.) at 0°. After 16 hr. at 0° the mixture was poured into ice-water. The resulting syrup (5·7 g.) was washed repeatedly with water, then with light petroleum. Recrystallization of the resulting solid from methanol gave needles of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside monotrichloroacetate* (0·76 g.), m. p. 206—207°, $[\alpha]_D^{20}$ +110° (*c*, 1·0 in $CHCl_3$) (Found : C, 36·0; H, 4·2. $C_{11}H_{15}O_7Cl_3$ requires C, 36·1; H, 4·1%).

Preparation of Esters of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside*.—(1) 2 : 3-*Dimethanesulphonate*. Methanesulphonyl chloride (85 g.) was added slowly to a solution of methyl 4 : 6-*O*-benzylidene-α-D-glucoside (70 g.) in pyridine (200 ml.), cooled in ice, and the mixture was kept at 0° for 20 hr. The product recrystallized from chloroform as prisms of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*dimethanesulphonate* (103 g.), m. p. 188—189°, $[\alpha]_D^{20}$ +49° (*c*, 1·4 in $CHCl_3$) (Found : C, 43·6; H, 5·1. $C_{16}H_{22}O_{10}S_2$ requires C, 43·8; H, 5·0%).

(2) 2-*Toluene*-p-*sulphonate*. The solution obtained by mixing toluene-*p*-sulphonyl chloride (9·5 g.) in pyridine (10 ml.) with methyl 4 : 6-*O*-benzylidene-α-D-glucoside (14 g.) in pyridine (10 ml.) was kept at 0° for 22 hr. Most of the solid obtained by stirring the mixture into ice-water dissolved when it was boiled with aqueous potassium carbonate (200 ml.; 2%). The insoluble part was filtered off, and when the filtrate cooled unchanged starting compound (6·9 g.), m. p. 162—163°, was obtained. The residue, washed with water, and recrystallized twice from methanol, gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-toluene-*p*-sulphonate (2·1 g.), $[\alpha]_D^{22}$ +63·5° (*c*, 0·9 in $CHCl_3$), m. p. 155°.

(3) 2 : 3-*Sulphite*. Thionyl chloride (6·5 ml., 1·5 mol.) was added gradually to a solution of glucoside (10 g.) in pyridine (50 mol.) at 0°. After 15 min. at 0° the mixture was poured into ice-water, giving a solid (10·5 g.) which was recrystallized twice from ethanol–acetone, yielding crystals (3·6 g.), m. p. 187—192°. A further recrystallization gave stout needles of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*sulphite*, m. p. 192—193°, $[\alpha]_D^{22}$ +148·4° (*c*, 0·9 in $CHCl_3$) (Found : C, 51·0; H, 5·1. $C_{14}H_{16}O_7S$ requires C, 51·2; H, 4·9%). The compound decomposes at room temperature.

(4) 2 : 3-*Dibenzenesulphinate*. A solution of the glucoside (5·6 g.) and sodium benzenesulphinate (9·8 g.) in acetic anhydride (30 ml.) was heated on a steam-bath. A solid began to separate after 30 min., and heating was continued for 18 hr. before the mixture was poured into ice-water. The resulting crystalline solid was dried, and recrystallized from methanol as plates of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*dibenzenesulphinate* (6·15 g.), m. p. 115—116°, $[\alpha]_D^{20}$ +44·1° (*c*, 1·3 in $CHCl_3$) (Found : C, 58·5; H, 5·3. $C_{26}H_{26}O_6S_2$ requires C, 58·9; H, 4·9%). Concentration of the recrystallization mother-liquor gave more compound (1·44 g.). When this preparation was carried out with reaction times of 30 min. and 3 hr., a syrup was obtained on pouring the mixture into ice-water. Only in the latter case was a small amount of the dibenzenesulphinate (17%) obtained. Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-diacetate (3·7 g.), sodium benzenesulphinate (4·9 g.), and acetic anhydride (15 ml.) were heated at 100°. A precipitate was immediately formed, and after 30 min. at 100° the mixture was decomposed with ice-water. The resulting solid, recrystallized from methanol, was methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dibenzenesulphinate (3·8 g.), m. p. and mixed m. p. 116—117°.

(5) 2 : 3-*Dichloroacetate*. The glucoside (5 g.), chloroacetic anhydride (15 g.), and sodium

chloroacetate (1·5 g.) were heated at 100° for 1 hr. The white solid obtained on pouring the mixture into iced potassium carbonate solution was recrystallized from methanol, yielding fine needles of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2 : 3-*dichloroacetate* (5·9 g.), m. p. 147°, $[\alpha]_D^{26}$ +67·3° (*c*, 1·1 in $CHCl_3$) (Found : C, 50·0; H, 4·4. $C_{15}H_{20}O_8Cl_2$ requires C, 49·7; H, 4·6%).

Reaction between Acetic Anhydride and Sodium Benzenesulphinate.—When sodium benzenesulphinate (8·2 g.) and acetic anhydride (30 ml.) were mixed at room temperature, an exothermic reaction took place accompanied by dissolution of the sodium salt and precipitation of another solid. The mixture after 20 hr. at 100° was poured into ice-water, to yield a syrup which crystallized. This solid (3·26 g.) recrystallized from light petroleum as long needles of phenyl benzenethiolsulphonate (1·67 g.), m. p. 35—36° (Found : C, 57·6; H, 4·0; S, 25·7. Calc. for $C_{12}H_{10}O_2S_2$: C, 57·6; H, 4·0; S, 25·6%). This compound, when mixed with an authentic sample, m. p. 43—44°, supplied by Dr. Cymerman-Craig, had m. p. 43—44°. Further recrystallization and seeding with the higher-melting form gave the compound with m. p. 43—44°. The reaction, repeated with benzene (4·5 ml.) or anisole (5 ml.) also present, again gave phenyl benzenethiolsulphonate (1·1 g.), m. p. 35—36°.

Preparation of Methyl 4 : 6-O-*Propylidene*-α-D-*glucoside* 3-*Nitrate* 2-*Toluene*-p-*sulphonate.*—Methyl 4 : 6-*O*-propylidene-α-D-glucoside 2 : 3-dinitrate (2 g.) was boiled under reflux for 18 hr. with sodium nitrite (1 g.) in ethanol (20 ml.) and water (5 ml.). Chloroform and water were then added. Evaporation of the chloroform layer gave a solid which, recrystallized from light petroleum (b. p. 80—100°), was crude methyl 4 : 6-*O*-propylidene-α-D-glucoside 3-nitrate (1·3 g.), m. p. 148—156°. This and toluene-*p*-sulphonyl chloride (1·3 g.) were kept at room temperature for 4 days in pyridine (10 ml.). The solid product, recrystallized twice from ethanol, gave methyl 4 : 6-*O*-propylidene-α-D-glucoside 3-nitrate 2-toluene-*p*-sulphonate (1·39 g.), m. p. 99°, $[\alpha]_D^{16}$ +109·5° (*c*, 0·9 in $CHCl_3$).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Propylidene*-α-D-*glucoside* 3-*Nitrate* 2-*Toluene*-p-*sulphonate.*—A solution of the 3-nitrate 2-toluene-*p*-sulphonate (1 g.) in methanol (20 ml.) containing sodium methoxide in methanol (2·7 ml.; 2·6N), was boiled under reflux for 1·5 hr. The dark solution was neutralized with acetic acid and evaporated. The residue, after extraction with boiling benzene, contained nitrite. The cooled benzene solution, chromatographed on alumina, gave from the first fractions starting compound (0·10 g.), m. p. and mixed m. p. 99—100°. Further elution with benzene–chloroform (1 : 1) yielded a sticky solid (0·24 g.), which was recrystallized from light petroleum to give methyl 4 : 6-*O*-propylidene-α-D-glucoside 3-nitrate (0·08 g.). No product was obtained by elution with ethanol. The light petroleum recrystallization mother-liquor was evaporated and the residue in benzene was re-chromatographed. This gave crude methyl 2 : 3-anhydro-4 : 6-*O*-propylidene-α-D-alloside (0·025 g.), m. p. 124—126°, mixed m. p. with pure compound (m. p. 136°), 126—129° (Found : C, 54·7; H, 7·4. Calc. for $C_{10}H_{16}O_5$: C, 55·6; H, 7·4%).

Conversion of Methyl 2 : 3-*Anhydro*-4 : 6-O-*benzylidene*-α-D-*alloside into the* 4 : 6-O-*Propylidene Analogue.*—A solution of methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·9 g.) in propaldehyde (10 ml.) and concentrated sulphuric acid (2 drops) was kept at room temperature for 30 min. The solution was neutralized with potassium carbonate and filtered, and the residue was washed with chloroform. The combined filtrate and washings, evaporated almost to dryness, left a residue, which, crystallized from ethanol–light petroleum, was methyl 2 : 3-anhydro-4 : 6-*O*-propylidene-α-D-alloside (0·46 g.), identical with that prepared by Ansell and Honeyman (*loc. cit.*).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Ethylidene*-α-D-*glucoside* 2 : 3-*Dinitrate.*—The 2 : 3-dinitrate (1·4 g.) was boiled under reflux for 24 hr. in methanol (40 ml.), containing sodium (0·2 g.). The dark mixture, which smelled strongly of paraldehyde and contained nitrite, was neutralized with acetic acid and evaporated to a syrup. The filtered chloroform extract of this was evaporated to a brown syrup, which apart from a little tar was dissolved in benzene and chromatographed on alumina. Nothing was eluted with benzene but elution with chloroform gave methyl 4 : 6-*O*-ethylidene-α-D-glucoside 3-nitrate (0·10 g.). No products were eluted with ethanol.

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Dichloroacetate*, 2 : 3-*Sulphite, and* 2 : 3-*Dibenzenesulphinate.*—Sodium methoxide in methanol (16 ml.; 2·6N) was added to the 2 : 3-dichloroacetate (3·7 g.) in chloroform (62 ml.) and the mixture was kept at 0° for 3 days. The chloroform solution was then shaken with water (3 × 50 ml.) and evaporated to a solid (2·05 g.), m. p. 158—162°, which after recrystallization from water was methyl 4 : 6-*O*-benzylidene-α-D-glucoside.

The analogues gave the same product.

Acid Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Sulphite*.—A solution of the sulphite (1 g.) in acetone (50 ml.) and water (4 ml.) containing hydrogen chloride (0·001N) was kept at room temperature for 30 min. The large crystals which had separated were collected, washed with acetone, and identified as methyl α-D-glucoside, m. p. and mixed m. p. 164—165°, $[\alpha]_D^{19}$ +158·2° (*c*, 0·2 in H_2O).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Dimethanesulphonate*.—This 2 : 3-dimethanesulphonate (14·8 g.) was dissolved in chloroform (250 ml.), and sodium methoxide in methanol (63 ml.; 2·6N) was added. The solution was kept for 20 hr. at 0° and then shaken with water until the washings were no longer alkaline. The dried chloroform solution was evaporated to a syrup, which was shaken with cold methanol (50 ml.). The residue (6·5 g.) was filtered off and washed with a little cold methanol. Evaporation of the filtrate and methanolic washings left a solid which, recrystallized from chloroform–light petroleum, was *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 3-*methanesulphonate* (4·3 g.), m. p. 142—143°, $[\alpha]_D^{17}$ +90° (*c*, 1·0 in $CHCl_3$) (Found : C, 50·0; H, 5·5; S, 9·2. $C_{15}H_{20}O_8S$ requires C, 50·0; H, 5·6; S, 8·9%). Concentration of the recrystallization liquors gave a further 0·4 g. Recrystallization of the above residue from chloroform gave unchanged starting compound (3·7 g.), m. p. and mixed m. p. 188—189°. Concentration of the chloroform gave a mixture of starting compound and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside.

In another experiment, the same reaction mixture, in half the above quantities, was left for 6 days at 0° and one day at room temperature, then treated as before. It gave, from the chloroform solution, a white solid which, after recrystallization from chloroform–light petroleum, was methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (2·35 g.). The mother-liquor from this recrystallization was evaporated, and the residue was extracted with methanol (20 ml.), leaving a solid which, after recrystallization, was shown to be anhydro-alloside (0·5 g.). Evaporation of the methanol solution gave a syrup which, crystallized from chloroform–light petroleum, was methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-methanesulphonate (0·53 g.).

Characterization of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Methanesulphonate*.—(*a*) Methanesulphonyl chloride (4 drops) was added to a solution of the 3-methanesulphonate (0·15 g.) in pyridine (1 ml.), and the mixture was kept at 0° for 20 hr. The solid, recrystallized from methanol, was methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dimethanesulphonate (0·13 g.), m. p. 188°.

(*b*) A suspension of the 3-methanesulphonate (1·5 g.) in acetic anhydride (2 ml.) was mixed at 0° with fuming nitric acid (0·5 ml.) dissolved in acetic anhydride (2 ml.). The solid rapidly dissolved, and after 5 min. the product began to separate. Precipitation was completed 10 min. later by addition of ice-water. Recrystallization of the washed and dried product from methanol–acetone gave needles of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 3-*methanesulphonate* 2-*nitrate* (1·34 g.), m. p. 185°, $[\alpha]_D^{16}$ +75° (*c*, 1·0 in $CHCl_3$) (Found : C, 45·0; H, 4·6; N, 3·3. $C_{15}H_{19}O_{10}NS$ requires C, 44·5; H, 4·7; N, 3·5%).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—(*a*) The 2 : 3-ditoluene-*p*-sulphonate (10 g.) in chloroform (125 ml.) was mixed with sodium methoxide in methanol (31·5 ml.; 2·6N) at 0°. After 17 hr. at this temperature, the solution was shaken with water (3 × 100 ml.), the last aqueous extract being neutral to litmus. The chloroform solution was evaporated and the resulting solid was washed with cold methanol (10 ml.). The solid was then extracted with cold benzene (20 ml.). Evaporation of the benzene, followed by recrystallization of the resulting solid from benzene, gave *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 3-*toluene*-p-*sulphonate* (1·27 g.), m. p. 164°, $[\alpha]_D^{23}$ +32·5° (*c*, 0·9 in $CHCl_3$) (Found : C, 58·6; H, 5·7; S, 7·7. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·5; S, 7·4%).

(*b*) A similar mixture containing 2 : 3-ditoluene-*p*-sulphonate (50 g.) was kept at 0° for 2 days. The crude product obtained in the same way was extracted with benzene (5 × 100 ml.) at room temperature. The residue, recrystallized from benzene, was methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (6·55 g.), m. p. 198—199°. The solid obtained by evaporation of the benzene extracts was dissolved in hot methanol (100 ml.). The cooled filtered solution deposited crystals which, twice recrystallized from benzene, were methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-toluene-*p*-sulphonate (3·75 g.). The benzene mother-liquors from the recrystallizations of the 3-toluene-*p*-sulphonate were combined and evaporated, and fuming nitric acid (5 ml.) in acetic anhydride (20 ml.) was added to the resulting solid suspended in acetic anhydride (20 ml.) at 0°. After 15 min. at 0°, undissolved solid was filtered off, washed with water, dried, and shown to be the anhydro-alloside (1·2 g.), m. p. 196—198°. The reaction solution was poured into ice-water, and the precipitated solid was recrystallized twice from ethanol–acetone, giving methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate 3-toluene-*p*-sulphonate (2·84 g.), m. p.

and mixed m. p. with authentic compound described below, 155—156°. Evaporation of the mother-liquors gave a solid which, purified by chromatography of its benzene solution on alumina, gave more (0·54 g.) of the 2-nitrate 3-toluene-*p*-sulphonate.

Characterization of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Toluene*-p-*sulphonate.*—Toluene-*p*-sulphonyl chloride (0·3 g.) was added to the 3-toluene-*p*-sulphonate (0·5 g.) in pyridine (2 ml.), and the mixture was kept at room temperature for 4 days. The product, recrystallized twice from ethanol, gave the 2 : 3-ditoluene-*p*-sulphonate (0·37 g.), m. p. 146—147°.

A suspension of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-toluene-*p*-sulphonate (0·94 g.) in acetic anhydride (2 ml.) dissolved after the addition of fuming nitric acid (0·5 ml.) in acetic anhydride (2 ml.) at 0°. The product obtained after 15 min. recrystallized from methanol as plates (0·73 g.), m. p. 153—155°. Another recrystallization gave *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2-*nitrate* 3-*toluene*-p-*sulphonate*, m. p. 155—156°, $[\alpha]_D^{19}$ +45·4° (*c*, 1·0 in $CHCl_3$) (Found : C, 52·8; H, 4·7; N, 2·9. $C_{21}H_{23}O_{10}SN$ requires C, 52·4; H, 4·8; N, 2·9%). This m. p. was depressed to 130—140° when the compound was mixed with methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate 2-toluene-*p*-sulphonate, m. p. 161—162°, the preparation of which is described below.

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2 : 3-*Dinitrate.*—(*a*) A 2·6N-solution of sodium methoxide in methanol (31·5 ml.) was added to methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate (6·3 g.), dissolved in chloroform (125 ml.), and the mixture was left at 0° for 3 days. The chloroform solution was then washed free from alkali with water (3 × 100 ml.) and evaporated. The solid left after extraction of the residue with boiling light petroleum (100 ml.) was recrystallized from methanol, to give needles of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 3-*nitrate* (1·55 g.), m. p. 174°, $[\alpha]_D^{23}$ +113·5° (*c*, 1·0 in $CHCl_3$) (Found : C, 51·4; H, 4·9; N, 3·9. $C_{14}H_{17}O_8N$ requires C, 51·4; H, 5·2; N, 4·3%). The cooled light petroleum extract deposited crystals (1·6 g.) which, recrystallized twice from methanol, were starting compound (0·70 g.).

(*b*) The same reaction mixture was left at room temperature for 5 days. The inorganic precipitate was then filtered off and found to contain much nitrite. The chloroform solution was washed with water (3 × 100 ml.). The first aqueous washing, which extracted the yellow colour from the chloroform and smelled strongly of benzaldehyde, had α_D +1·8° (2 dm. tube). The second and third aqueous washings were colourless and optically inactive. The chloroform solution was evaporated to yield a sticky solid, which was extracted with boiling light petroleum (25 ml.). The solid which remained recrystallized from methanol, to give methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate (0·7 g.). The brown unstable solid, obtained by evaporation of the methanolic mother-liquor at room temperature, was extracted with hot carbon tetrachloride. The cooled, concentrated carbon tetrachloride solution deposited needles (0·3 g.), which, recrystallized from methanol, gave more 3-nitrate (0·16 g.). The light petroleum extract was evaporated to a syrup which was dissolved in ether, and chromatographed on alumina. Elution with ether gave, in the early fractions, unchanged starting compound (1·0 g.). Later fractions gave, after evaporation and recrystallization of the residue from chloroform–light petroleum, *methyl* 4 : 6-*O*-*benzylidene*-α-D-*glucoside* 2-*nitrate* (0·35 g.), m. p. 136°, $[\alpha]_D^{24}$ +109·6° (*c*, 0·57 in $CHCl_3$) (Found : C, 51·9; H, 5·7; N, 3·8. $C_{14}H_{17}O_8N$ requires C, 51·4; H, 5·2; N, 4·3%). Elution with ether–chloroform (1 : 1) and finally with chloroform gave the 3-nitrate (0·32 g.). No further products were obtained when the column was washed with ethanol.

(*c*) A 2·6N-solution of sodium methoxide in methanol (3·6 ml.) was boiled with the 2 : 3-dinitrate (1·2 g.) in methanol (10 ml.) for 1 hr. under reflux. The dark solution was neutralized with acetic acid, and evaporated. Extraction of the residue with chloroform, followed by evaporation of the extract, gave a syrup which was chromatographed in benzene on alumina. Successive elution with benzene, chloroform, and ethanol gave methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·03 g.), methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate (0·02 g.), and methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·02 g.).

(*d*) The dinitrate (6·3 g.) and *o*-phenylene diamine (2·8 g.) were dissolved in chloroform (125 ml.), and sodium methoxide in methanol (31·5 ml.; 2·6N) was added. After 4 days at room temperature, the chloroform solution was washed free from alkali with water (3 × 100 ml.), and then evaporated to a syrup, most of which dissolved in methanol. The undissolved solid was purified by precipitation from chloroform with light petroleum, giving the *quinoxaline derivative* of methyl 4 : 6-*O*-benzylidene-2 : 3-dideoxy-2 : 3-dioxo-α-D-glucoside (0·11 g.), $[\alpha]_D^{18}$ −90° (*c*, 0·3 in $CHCl_3$) (Found : C, 68·8; H, 5·0; N, 7·8. $C_{20}H_{18}O_4N_2$ requires C, 68·6; H, 5·1; N, 8·0%). This compound decomposed between 230° and 240° without melting.

Characterization of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Nitrate*.—Fuming nitric acid (0·5 ml.) in acetic anhydride (1·5 ml.) was added slowly to a suspension of the 3-nitrate (0·5 g.) in acetic anhydride (1·5 ml.), at 0°. The resulting solid, recrystallized from methanol, gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate (0·36 g.), m. p. 122—123°.

A suspension of the 3-nitrate (0·1 g.) in paraldehyde (1 ml.) and concentrated sulphuric acid (0·2 drop) was shaken until the solid had dissolved (5 min.). The mixture was left for 30 min. more at room temperature, then chloroform and potassium carbonate were added. Evaporation of the filtered solution gave a solid (0·06 g.), which was recrystallized from ether–light petroleum as fine needles of methyl 4 : 6-*O*-ethylidene-α-D-glucoside 3-nitrate, m. p. 176°.

Characterization of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2-*Nitrate*.—A mixture of methanesulphonyl chloride (0·1 g.), the 2-nitrate (0·1 g.), and pyridine (1 ml.) was kept for 20 hr. at 0°. The product yielded a solid (0·09 g.), which after two recrystallizations from methanol was shown to be methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-methanesulphonate 2-nitrate, m. p. 185°.

Derivatives of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Nitrate*.—(*a*) Fused sodium acetate (1 g.), 3-nitrate (2 g.), and acetic anhydride (10 ml.) were heated together for 1 hr. at 100° and then poured into ice-water. The resulting solid was recrystallized from light petroleum, to give thin plates of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2-*acetate* 3-*nitrate* (1·83 g.), m. p. 110°, $[\alpha]_D^{18}$ +83·7° (*c*, 1·0 in $CHCl_3$) (Found : C, 51·8; H, 5·3. $C_{16}H_{19}O_9N$ requires C, 52·0; H, 5·2%).

(*b*) A solution of the 3-nitrate (1 g.) and toluene-*p*-sulphonyl chloride (1 g.) in pyridine (5 ml.) was left at room temperature for 5 days. The product, recrystallized from methanol, was thin plates of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 3-*nitrate* 2-*toluene*-p-*sulphonate* (1·15 g.), m. p. 161—162°, $[\alpha]_D^{16}$ +59° (*c*, 0·9 in $CHCl_3$) (Found : C, 52·2; H, 5·0; S, 6·7. $C_{21}H_{23}O_{10}NS$ requires C, 52·4; H, 4·8; S, 6·7%).

(*c*) Methanesulphonyl chloride (3 ml.) was added dropwise to a solution of the 3-nitrate (5 g.) in pyridine (25 ml.) at 0°. The mixture was kept at 0° for 20 hours. Recrystallized from methanol, the product yielded needles of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2-*methanesulphonate* 3-*nitrate* (5·82 g.), m. p. 129—130°, $[\alpha]_D^{15}$ +68·8° (*c*, 1·0 in $CHCl_3$) (Found : C, 44·8; H, 4·9. $C_{15}H_{19}O_{10}NS$ requires C, 44·5; H, 4·7%).

(*d*) Silver oxide (6 g.) was added in portions during 3 hr. to a suspension of the 3-nitrate (3 g.) in boiling methyl iodide (15 ml.). The mixture was boiled for a further 19 hr. before the silver residue was filtered off. The residue was washed with methanol, and the washings and filtrate were combined and evaporated. The resulting solid (3 g.), m. p. 114—115°, recrystallized from light petroleum, was *methyl* 4 : 6-O-*benzylidene*-2-O-*methyl*-α-D-*glucoside* 3-*nitrate*, m. p. 116—117°, $[\alpha]_D^{20}$ +83·7° (*c*, 1·0 in $CHCl_3$) (Found : C, 53·4; H, 5·6. $C_{15}H_{19}O_8N$ requires C, 52·8; H, 5·6%).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Nitrate*.—(*a*) A 2·6N-solution of sodium methoxide in methanol (9 ml.) was added to a solution of carefully purified methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate (1·5 g., 1 mol.) in chloroform (37·5 ml.), and the mixture was kept for 7 days at room temperature. The colourless mixture was then shaken with water to remove alkali. Sodium nitrite was present in the aqueous layer. Evaporation of the chloroform layer gave a solid, which was chromatographed on alumina in benzene. The first fractions eluted with benzene gave an unidentified syrup (0·13 g.), then, after a distinct break, more syrup was obtained, which crystallized from light petroleum as granular crystals of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate (0·07 g.), m. p. and mixed m. p. 134—135°. Subsequent fractions, including those obtained by washing the column with chloroform, were combined and recrystallized from carbon tetrachloride to give unchanged 3-nitrate (0·66 g.), m. p. and mixed m. p. 171—172°. A mixture of the 3-nitrate (0·02 g.), m. p. 174°, and the 2-nitrate (0·001 g.), m. p. 136°, softened at 130°, and melted at 145—165°.

(*b*) Sodium methoxide in methanol (2·4 ml.; 2·6N) was boiled under reflux for 1 hr. with the 3-nitrate (1 g.) in methanol (10 ml.). The brown solution, cooled to 0°, deposited methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·17 g.). The filtered solution, after neutralization with acetic acid, was evaporated to a residue, whose chloroform extract was chromatographed on alumina. The early fractions eluted by chloroform gave solid (0·19 g.), which, twice recrystallized from carbon tetrachloride, was unchanged 3-nitrate (0·11 g.). Subsequent fractions, including that obtained by washing of the column with ethanol, were combined and identified as methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·30 g.).

(*c*) 3-Nitrate (2 g.) in methanol (40 ml.) was boiled for 24 hr. with sodium methoxide in

methanol (4·7 ml.; 2·6N). The dark, neutralized solution was evaporated to a tar which was extracted with chloroform (50 ml.). Evaporation of the chloroform solution left a brown, partly solid mass, which was chromatographed on alumina (70 g.) in chloroform solution. First fractions gave, after recrystallization from methanol, methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·15 g.). Subsequent fractions yielded an unidentified syrup (0·36 g.). When the column was washed with alcohol methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·60 g.) was obtained.

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-2-O-*methyl*-α-D-*glucoside* 3-*Nitrate*.—Sodium methoxide in methanol (2·4 ml.; 2·6N) was boiled under reflux for 1 hr. with methyl 4 : 6-*O*-benzylidene-2-*O*-methyl-α-D-glucoside 3-nitrate (1 g.) in methanol (10 ml.). The dark, cold solution deposited crystals of starting compound (0·54 g.). The mother-liquor, neutralized with acetic acid, was evaporated to a solid, to which chloroform was added. The insoluble inorganic residue, containing nitrite, was filtered off. Evaporation of the filtrate left a residue, which was chromatographed in benzene solution on alumina. First fractions eluted with benzene gave a solid which, recrystallized from light petroleum, was starting compound (0·12 g.). When the eluant was changed to chloroform, a solid (0·08 g.) was obtained, which was recrystallized from chloroform–light petroleum and identified as methyl 4 : 6-*O*-benzylidene-2-*O*-methyl-α-glucoside, m. p. 166—168°, undepressed on admixture with an authentic sample supplied by Dr. D. J. Bell.

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Nitrate* 2-*Toluene*-p-*sulphonate*.—(*a*) The 3-nitrate 2-toluene-*p*-sulphonate (1·0 g.) in chloroform (10 ml.) was mixed with sodium methoxide in methanol (2·0 ml.; 2·6N) and kept for 24 hr. at 0°. The solution, diluted with chloroform, was washed free from alkali with water and evaporated. The aqueous washings, which contained nitrite, were optically inactive. Evaporation of the chloroform solution left a residue which was chromatographed in ether on alumina. The first fractions eluted with ether gave a solid (0·45 g.), which, after recrystallization from methanol, yielded starting compound (0·25 g.). Further elution with ether–chloroform gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-nitrate (0·22 g.).

(*b*) Sodium methoxide in methanol (3·6 ml.; 2·6N) was added to the ester (1·5 g.) in chloroform (10 ml.), and the mixture was kept at 0° for 48 hr. The crude products were isolated as in (*a*) and chromatographed in benzene on alumina. Benzene, followed by chloroform, eluted starting compound (0·17 g.), methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate (0·10 g.), and the 3-nitrate (0·37 g.).

(*c*) The quantities of reactants used in (*b*) but dissolved in methanol (10 ml.) only were boiled under reflux for 1·75 hr. Methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·5 g.) was deposited from the cooled solution, neutralized with acetic acid. The residue from the evaporated solution was extracted with chloroform, and the chloroform solution was evaporated to a dark syrup, which was chromatographed from benzene on alumina. After an unidentified syrup (0·07 g.), the benzene eluate yielded crystals (0·015 g.) which, recrystallized, proved to be the anhydro-alloside. Elution with chloroform gave slightly impure 3-nitrate (0·03 g.), m. p. and mixed m. p. 169—170°, and finally elution with ethanol gave crystals (0·12 g.) which, recrystallized from chloroform–light petroleum, were methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·09 g.).

(*d*) The ester (2 g.) in methanol (50 ml.), and sodium methoxide in methanol (4·8 ml.; 2·6N), were boiled under reflux for 24 hr. The dark brown solution was then neutralized with acetic acid and evaporated. The residue, containing nitrite, was extracted with chloroform (50 ml.), and the chloroform solution was chromatographed on alumina. First fractions yielded, after recrystallization from chloroform–light petroleum, methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·06 g.). Subsequent elution with ethanol followed by recrystallization from water gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·13 g.).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2-*Nitrate* 3-*Toluene*-p-*sulphonate*.—(*a*) The 2-nitrate 3-toluene-*p*-sulphonate (1·5 g.) in chloroform (10 ml.) was kept with sodium methoxide in methanol (3·6 ml.; 2·6N), at 0° for 48 hr. The colourless solution was diluted with chloroform, washed with water, and evaporated to a solid. The aqueous washings contained nitrite, and had a small positive optical rotation. A benzene solution of the solid was chromatographed on alumina. Benzene eluted first unchanged starting compound (0·19 g.), then a solid (0·40 g.), which, recrystallized from benzene, gave methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·26 g.). Final elution with chloroform gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-toluene-*p*-sulphonate (0·13 g.).

(*b*) The ester (1·5 g.) in methanol (10 ml.) was boiled under reflux with sodium methoxide

in methanol (3·6 ml.; 2·6N) for 1·5 hr. The dark solution, on cooling, deposited methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (0·16 g.). The filtrate was neutralized with acetic acid and evaporated to a syrup, whose benzene solution was chromatographed on alumina. No products were eluted with benzene, but with chloroform more anhydro-alloside (0·015 g.) was obtained, followed by a syrup (0·45 g.). No products were eluted with ethanol. The syrup was dissolved in chloroform–benzene (1 : 1) and rechromatographed, this solvent mixture being used as eluant. The resulting syrup crystallized (0·38 g.), and was recrystallized several times from ether–light petroleum, to give an unidentified product, m. p. 112° (Found : C, 59·5; H, 6·65%).

Alkaline Hydrolysis of Methyl α-D-Glucoside 2 : 3 : 4-Triacetate 6-Nitrate.—Sodium methoxide in methanol (12·5 ml.; 2·6N) was added to methyl α-D-glucoside 2 : 3 : 4-triacetate 6-nitrate (2·47 g.) in methanol (62·5 ml.), and the solution was boiled under reflux for 24 hr. The solution was neutralized with glacial acetic acid and then evaporated. The filtered chloroform solution of the residue, chromatographed on alumina, yielded a product (0·88 g.), m. p. 103—106°, which after recrystallization from chloroform–light petroleum was methyl 3 : 6-anhydro-α-D-glucopyranoside, m. p. 106—108°, $[\alpha]_D^{18}$ +53° (*c*, 0·1 in H_2O).

Reactions of Methyl 4 : 6-O-Benzylidene-α-D-glucoside 2 : 3-Dinitrate.—(a) *With sodium iodide in acetone.* Sodium iodide (21 g.) and the 2 : 3-dinitrate (10·5 g.) were boiled in acetone (87 ml.) for 20 hr. Nitric oxide was evolved, and iodine was liberated. Evaporation of the acetone gave a nitrite-containing lachrymatory solid, which was extracted several times with chloroform. The combined extracts were washed with water and with aqueous sodium thiosulphate, decolorized with charcoal, and evaporated. The residue was extracted with boiling light petroleum (100 ml.), and the insoluble portion was recrystallized from carbon tetrachloride to yield 3-nitrate (4·4 g.). When the light petroleum extract was cooled, a syrup separated, which partly crystallized. Recrystallization from methanol gave prisms of starting compound (1·35 g.).

(b) *With sodium iodide in methanol.* A sealed tube containing the 2 : 3-dinitrate (2 g.) and sodium iodide (2 g.) dissolved in methanol (15 ml.) was heated at 100° for 20 hr. Chloroform and water were added and the mixture was titrated with 0·2036N-sodium thiosulphate. The chloroform layer was then separated, and the aqueous layer was extracted once more with chloroform. Water was added to the aqueous layer to make 250 ml. Potassium iodide solution (10 ml.; 10%) was added to portions (50 ml.) of this solution, and nitrogen was bubbled through it. Hydrochloric acid (20 ml.; 2N) was introduced below the liquid surface, and the liberated iodine was titrated with 0·0504N-sodium thiosulphate. When a portion of the solution was boiled with ammonium chloride (1 g.) for 5 min. before addition of the potassium iodide and acid, no iodine was liberated.

The combined chloroform extracts were evaporated to a residue, whose benzene solution was chromatographed on alumina. The benzene eluant gave starting compound : the 3-nitrate was obtained when the column was subsequently eluted with chloroform. No further products were obtained on elution with ethanol. The compounds were identified by m. p. and mixed m. p. with an authentic specimen. The results are recorded in Table 1.

(c) *With sodium nitrite in aqueous ethanol.* The 2 : 3-dinitrate (8 g.) and sodium nitrite (4 g.) were boiled in ethanol (40 ml.) and water (10 ml.) for 21 hr. The solvent was evaporated, and the white solid residue was extracted with chloroform. The chloroform extracts were washed with water, and evaporated to a white solid, which was boiled with potassium carbonate solution (50 ml.; 2%). The solid which remained undissolved was filtered off and recrystallized from methanol, to give needles of 3-nitrate (4·96 g.). The solid obtained by concentration and cooling of the potassium carbonate solution was, after recrystallization from chloroform–light petroleum, methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·3 g.).

When the 2 : 3-dinitrate (2 g.) alone was boiled with aqueous ethanol for 20 hr., starting compound (1·7 g.) was the only product isolated.

Reactions of Methyl 4 : 6-O-Ethylidene-α-D-glucoside 2 : 3-Dinitrate.—(a) *With sodium iodide in acetone.* The 2 : 3-dinitrate (3 g.) in acetone (25 ml.) containing sodium iodide (6 g.) was heated in a sealed tube at 100° for 24 hr. The evaporated mixture was extracted with chloroform, and the extract was washed successively with water, sodium thiosulphate solution, and sodium hydrogen carbonate solution, and evaporated. The white solid (1·45 g.) obtained was recrystallized from ether–light petroleum as fine needles of 3-nitrate.

(b) *With sodium iodide in pyridine.* Sodium iodide (4 g.) and the 2 : 3-dinitrate (2 g.) were boiled for 30 min. in pyridine (20 ml.). Oxides of nitrogen were evolved, and iodine was liberated. When the mixture was poured into water, no solid separated but, when the solution

was concentrated and cooled, fine needles (0·92 g.) appeared. These, recrystallized from ether–light petroleum, were 3-nitrate. Concentration of the aqueous-pyridine solution gave more 3-nitrate (0·1 g.).

When the 2 : 3-dinitrate (2 g.) was heated to 100° for 30 min. in pyridine (20 ml.) alone, the solution darkened. The mixture was poured into ice-water; a solid (1·7 g.) separated, which recrystallized from light petroleum as stout needles (1·54 g.) of starting compound.

(c) *With sodium nitrite in aqueous ethanol.* A solution of the 2 : 3-dinitrate (4·3 g.) and sodium nitrite (2·5 g.) in ethanol (20 ml.) and water (5 ml.) was boiled for 17 hr. The concentrated solution was shaken with chloroform and water, and the chloroform layer was evaporated. The solid residue, recrystallized from ether, gave 3-nitrate (2·5 g.).

Attempted Reaction of Sulphonates and Acetate with Sodium Iodide.—(*a*) Methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate (2 g.) and sodium iodide (4 g.) were boiled for 17 hr. in dry pyridine (20 ml.). Pouring the mixture into ice-water gave a white solid which was filtered off and recrystallized from methanol as thin plates of starting compound (1·3 g.).

(*b*) When methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-diacetate (2·0 g.) was heated with sodium iodide in acetone in a sealed tube at 100° for 20 hr., starting compound (1·9 g.) was recovered.

(*c*) After similar treatment of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dimethanesulphonate (3·0 g.) with sodium iodide in acetone starting compound (2·5 g.) was obtained.

(*d*) After methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-ditoluene-*p*-sulphonate was heated with sodium iodide and acetone in a sealed tube at 100° for 21 hr. the starting compound (88%) was recovered.

Unchanged 2 : 3-ditoluene-*p*-sulphonate was also recovered (90%) after being boiled with sodium nitrite in ethanol for 48 hr.

Reactions of Sodium Iodide in Acetone with Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 3-*Nitrate*, 3-*Nitrate* 2-*Toluene*-p-*sulphonate*, 3-*Nitrate* 2-*Methanesulphonate*, *and* 2-*Acetate* 3-*Nitrate*.—A solution of the 3-nitrate (2 g.) and sodium iodide (4 g.) in acetone (15 ml.) was heated in a sealed tube at 100° for 20 hr. The solid obtained on evaporation was extracted with chloroform, and the chloroform solution was washed with water and aqueous sodium thiosulphate and decolorized with charcoal. Evaporation left a white solid, which was extracted with hot aqueous potassium carbonate (25 ml.; 2%). The insoluble part (1·22 g.), after recrystallization from methanol, was starting compound. The needles (0·37 g.), m. p. 160—161°, which separated from the cold potassium carbonate extract were, after recrystallization from chloroform–light petroleum, methyl 4 : 6-*O*-benzylidene-α-D-glucoside.

The 3-nitrate 2-toluene-*p*-sulphonate was treated as in the previous experiment. Chloroform and water were added to the evaporated reaction products, which did not include nitrite, and the mixture was then shaken with aqueous sodium thiosulphate. The chloroform layer was evaporated to a syrup which, crystallized and recrystallized from methanol, gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-toluene-*p*-sulphonate (1·19 g.).

The 2-methanesulphonate 3-nitrate (2 g.) was treated as in the previous experiments. Again the products did not contain nitrite. The washed chloroform extract afforded crystals which were washed with boiling light petroleum, and then recrystallized twice from methanol to give needles (1·31 g.) of *methyl* 4 : 6-O-*benzylidene*-α-D-*glucoside* 2-*methanesulphonate*, m. p. 132—133° (depressed to 105—115° when mixed with starting compound, m. p. 129—130°), $[\alpha]_D^{22}$ +72° (*c*, 1·2 in $CHCl_3$) (Found: C, 49·8; H, 5·4. $C_{15}H_{20}O_8S$ requires C, 50·0; H, 5·6%). The 2-acetate 3-nitrate (1·5 g.) was similarly treated. The residue obtained by evaporation of the reaction mixture was extracted with chloroform. The chloroform solution was washed with aqueous sodium thiosulphate and evaporated to a syrup, which, dissolved in benzene, was chromatographed on alumina. First fractions gave starting compound (0·51 g.). Further elution with chloroform gave a solid (0·61 g.), which was recrystallized from chloroform–light petroleum to give needles (0·28 g.), found after two more recrystallizations to be methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-acetate, m. p. 182°, $[\alpha]_D^{18}$ +115° (*c*, 0·9 in $CHCl_3$), mixed m. p. 174—180° with an authentic compound of m. p. 173° [Bourne *et al.* (*loc. cit.*)]. Concentration of the first recrystallization mother-liquor gave methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-acetate (0·09 g.), m. p. 131°, $[\alpha]_D^{17}$ +110° (*c*, 0·65 in $CHCl_3$), mixed m. p. 128—130° with an authentic sample of m. p. 128°.

Characterization of Methyl 4 : 6-O-*Benzylidene*-α-D-*glucoside* 2-*Methanesulphonate*.—Fuming nitric acid (0·2 ml.) in acetic anhydride (1·0 ml.) was added to a suspension of the 2-methanesulphonate (0·2 g.) in acetic anhydride (0·5 ml.) at 0°. After 15 min. at 0°, the mixture was

poured into ice-water, a syrup separating. The aqueous solution was decanted and sufficient hot methanol was added to dissolve the syrup. Cooling afforded needles of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-methanesulphonate 3-nitrate (0·07 g.), m. p. 126—127°, which after a recrystallization had m. p. and mixed m. p. 129°.

Reaction of Methyl 4 : 6-O-*Benzylidene-α-*D-*glucoside* 2 : 3-*Dinitrate with Pyridine containing Hydroxylamine Hydrochloride.*—When the 2 : 3-dinitrate (2 g.) in pyridine (20 ml.) was heated to 100° for 4·5 hr. crystals appeared in the condenser and brown fumes were evolved. No product separated when the dark brown mixture was poured into water.

When the 2 : 3-dinitrate (2 g.) in pyridine (20 ml.) containing hydroxylamine hydrochloride (2 g.) was heated at 100° for 4 hr. the solution was not coloured, no brown fumes were evolved, and pouring the mixture into water gave a syrup which solidified after several changes of water. This solid, recrystallized from ethanol–light petroleum, gave a compound (0·05 g.) which after recrystallization from chloroform was *methyl* 4 : 6-O-*benzylidene*-2 : 3-*dideoxy*-2 : 3-*dioxo*-α-D-*glucoside* 2 : 3-*dioxime* (Found : C, 54·4; H, 5·1; N, 8·6. $C_{14}H_{16}O_6N_2$ requires C, 54·5; H, 5·2; N, 9·1%). The compound sublimed in the m. p. tube at 170—180° and decomposed at 180°. Some starting compound was recovered from the recrystallization mother-liquors.

Extraction of the aqueous pyridine mother-liquor with chloroform gave, in both experiments, a dark syrup.

The dinitrate was recovered (77%) after 24 hr. at room temperature in pyridine containing hydroxylamine hydrochloride.

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N-*Substituted Glycosylamines. Part V.* Acetates and Benzoates.*

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The crystalline acetates and benzoates prepared from several *N*-arylaldosylamines are shown to be pyranose derivatives.

Unsuccessful attempts were made to characterize fully 1-deoxy-1-*p*-tolylamino-D-fructose.

N-Arylaldosylamines are readily prepared by condensing the appropriate sugar and amine and the methods used in this work are summarized in the Experimental section. Weygand, Perkow, and Kuhner's methods (*Chem. Ber.*, 1951, **84**, 594) have been convenient for making the stable *N*-*p*-nitrophenylaldosylamines; that from D-ribose is described for the first time. The nature and physical constants of these compounds confirm the German workers' results, except for D-xylose, from which they obtained two isomeric *N*-*p*-nitrophenyl-D-xylosylamines, considered to be a pyranose and furanose pair. During the present work only one form was obtained [that believed by Weygand *et al.* (*loc. cit.*) to be furanoid], and it was found to react on acetylation and benzoylation in the pyranose form

By a simple, general method of acetylation *N*-phenyl-D-mannosylamine, *N*-*p*-tolyl-D-galactosylamine, and *N*-*p*-nitrophenyl-D-glucosylamine, -D-mannosylamine, and -D-xylosylamine have been converted into sharp-melting, crystalline acetates. These are all pyranose because they were hydrolysed by dilute aqueous formic acid to the known, crystalline aldohexose 2 : 3 : 4 : 6-tetra-acetates or D-xylose 2 : 3 : 4-triacetates in yields of about 50%. The tetra-acetate obtained from *N*-*p*-tolyl-D-mannosylamine had a wide melting range and

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is a mixture; nevertheless, on hydrolysis it gave D-mannose 2 : 3 : 4 : 6-tetra-acetate only, and is, therefore, a mixture of pyranose anomers. This was substantiated by the preparation of the same mixture by condensing D-mannose 2 : 3 : 4 : 6-tetra-acetate with *p*-toluidine. Since the completion of this work Bognár and Nánási (*J.*, 1955, 185) have separated the mixture into two isomeric tetra-acetates. *N*-*p*-Nitrophenyl-D-galactosylamine also gives a tetra-acetate with a wide melting range : the same compound has been prepared by Frèrejacque (*Compt. rend.*, 1938, **207**, 638) who did not record a melting point. Again, the product is considered to be a mixture of pyranose anomers.

Nitration of *N*-*p*-tolyl-β-D-glucosylamine tetra-acetate with fuming nitric acid in acetic anhydride gave *N*-(2-nitro-*p*-tolyl)-D-glucosylamine tetra-acetate,* previously prepared by a different method. This structure was verified by hydrolysis of the compound to 2-nitro-*p*-toluidine. Further nitration of the mononitro-compound yielded a dinitro-derivative, hydrolysed to 2 : 6-dinitro-*p*-toluidine. This suggests that the structure is *N*-(2 : 6-dinitro-*p*-tolyl)-D-glucosylamine tetra-acetate but because migration of a nitro-group from the amino-nitrogen atom to the benzene ring can occur under the acid conditions used for hydrolysis the compound is as likely to be D-glucosyl-2-nitro-*p*-tolylnitramine tetra-acetate. The position of the second nitro-group has, therefore, not been firmly established. Nitration of *N*-*p*-tolyl-β-D-glucosylamine tetra-acetate with fuming nitric acid in chloroform yielded a trinitro-derivative, which with diphenylbenzidine in concentrated sulphuric acid gave the blue colour characteristic of nitric acid, suggesting the presence of either an aromatic nitramine with the *o*- and *p*-positions substituted (see Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 50) or an ester nitrate. The latter is unlikely from the analysis and from the stability of acetates under the nitrating conditions. The most probable structure, *N*-D-glucopyranosyl-2 : 6-dinitro-*p*-tolylnitramine tetra-acetate, was confirmed by preparing it from 2 : 6-dinitro-*p*-tolylnitramine and D-glucopyranosyl bromide tetra-acetate.

Crystalline benzoates have been prepared by subjecting *N*-*p*-nitrophenyl-D-mannosylamine, -D-glucosylamine, -D-xylosylamine, and -L-arabinosylamine, and *N*-*p*-tolyl-D-galactosylamine to brief, mild treatment with benzoyl chloride in pyridine. Each gave one ester only, except *N*-*p*-nitrophenyl-D-glucosylamine from which a small amount of a second tetrabenzoate was also obtained. Because the latter was rapidly but partly converted into its isomer in methanolic hydrogen chloride solution these are considered to be anomeric. Each of the crystalline benzoates, except that from D-galactose, prepared from the above arylaldosylamines was hydrolysed to the corresponding aldohexopyranose tetrabenzoate or aldopentopyranose tribenzoate, all adequately characterized previously by preparation from the aldopyranosyl bromide benzoates.

Benzoylation of *N*-phenyl-D-mannosylamine and -D-xylosylamine, and *N*-*p*-nitrophenyl-D-ribosylamine, gave from each a non-crystalline product whose exact nature was uncertain. But the isolation from their hydrolysis product of only the crystalline D-mannopyranose tetrabenzoate, and D-xylopyranose and D-ribopyranose tribenzoates, respectively, showed that the parent aldosylamines had reacted, at least predominantly, in the pyranose form. The case of the two crystalline *N*-*p*-tolyl-D-ribosylamines designated *A* and *B* (Ellis and Honeyman, *J.*, 1952, 1490) is of particular interest. By benzoylating *B* with the temperature initially low (−70°), and purifying the crude product chromatographically, a good yield was obtained of *N*-*p*-tolyl-D-ribosylamine 2 : 3 : 4-tribenzoate, whose structure was proved by its hydrolysis to D-ribose 2 : 3 : 4-tribenzoate. Isomer *A* gave the same tribenzoate. Solutions of both *A* and *B* in pyridine containing hydrogen chloride mutarotated rapidly to a common equilibrium value. These conditions exist during benzoylation and consequently the above tribenzoate is derived from a constituent of the equilibrium solution and not necessarily from either *A* or *B*. These findings are strong support for the belief that the poorly characterized compounds, one of $[\alpha]_D^{28}$ −22·1° (*c*, 8 in pyridine) and the other of $[\alpha]_D^{28}$ −20·3° (±1°) (*c*, 1·67 in pyridine), which Berger and Lee (*J. Org. Chem.*, 1946, **11**, 75) obtained by benzoylating the isomeric *N*-phenyl-D-ribosylamines and then hydrogenating the crude benzoates, are identical and not isomeric as

* In this and other toluidine derivatives recorded in this paper, the number 1 is assigned to the position in the aromatic ring carrying the amino-group (cf. *J.*, 1952, 5090, footnote 20).

originally stated. Since the same conditions exist during reaction with triphenylmethyl chloride serious doubt is cast on any conclusions regarding structure drawn from the preparation of trityl derivatives of *N*-arylpentosylamines (Berger and Lee, *loc. cit.*, and references therein).

Only few crystalline derivatives of the *N*-substituted 1-amino-1-deoxy-D-fructoses are known. Hodge and Rist (*J. Amer. Chem. Soc.*, 1953, **75**, 316) have prepared a mono-*O-iso*propylidene derivative of 1-deoxy-1-piperidino-D-fructose, and Helferich and Porck (*Annalen*, 1953, **582**, 233) have obtained 1-benzylamino-4 : 6-*O*-benzylidene-1-deoxy-D-fructose indirectly. Now, by shaking 1-deoxy-1-*p*-tolylamino-D-fructose with acetone containing concentrated sulphuric acid, the sulphate of a mono-*O-iso*propylidene derivative has been obtained. Treatment of this with ammonia gave the crystalline mono-*O-iso*-propylidene compound. (The authors are grateful to Dr. S. Bayne for communicating this process to them.) This derivative reduced Fehling's solution and 2 : 6-dichlorophenolindophenol, gave an oxime, and with phenylhydrazine gave an *O-iso*propylidene-D-glucosazone, so $C_{(2)}$ is unsubstituted. However, all attempts to methylate or esterify it by the methods successfully used for the *N*-arylglycosylamines have given syrups. An attempt was made to obtain further information about the compound by oxidizing it with sodium periodate in aqueous acetone. During the reduction of periodate the solution became dark; similar treatment of *p*-toluidine was found to involve the consumption of nearly the same amount of periodate with the same coloration. This surprising result, which shows that periodate oxidation is of doubtful value for structural studies on *N*-arylglycosylamines and the rearranged products, is now being studied in detail.

Unsuccessful attempts have been made to prepare crystalline ethers and esters of 1-deoxy-1-*p*-tolylamino-D-fructose.

Experimental

Chloroform solutions were washed with 0·5N-hydrochloric acid, sodium hydrogen carbonate solution, and water as required, and dried over sodium sulphate before being evaporated under reduced pressure. The light petroleum used had boiling range 60—80°. The alumina used for chromatography was "Activated Alumina, Type H," 100/200 S mesh, supplied by Messrs. Peter Spence and Sons Ltd.

General Methods for the Preparation of N-*Phenyl- and* N-p-*Tolyl-aldosylamines.*—(1) A solution of the sugar (5 g.) and the amine (5 g.) in ethanol (50 ml.) was boiled under reflux for 2 hr. and then cooled. The glycosylamine which crystallized was collected, washed with ethanol and with ether, and dried in a vacuum-desiccator.

(2) The amine (5 g.) in ethanol (12 ml.) was added to a solution of the sugar (5 g.) in 0·001N-sulphuric acid (10 ml.). This was left for 24 hr. and the crystalline product was collected and purified as in (1).

(3) A mixture of sugar (5 g.), amine (4 g.), and water (1·5 ml.) was heated on a steam-bath until homogeneous and then for 5 min. more. Ethanol (10 ml.) was added and, after cooling, the crystalline product was collected, washed with ethanol and with ether, and recrystallized from ethanol.

N-p-*Nitrophenylaldosylamines.*—Weygand, Perkow, and Kuhner's methods (*loc. cit.*) were used. The constants of the derivatives obtained from D-glucose, D-mannose, D-galactose, and L-arabinose were in good agreement with those recorded.

Preparation of N-p-*Nitrophenyl*-D-*xylosylamine.*—(1) A mixture of D-xylose (5 g.), *p*-nitroaniline (5 g.), water (1 ml.), methanol (10 ml.), and glacial acetic acid (0·1 ml.) was heated under reflux for 10 min. The solids gradually dissolved; the product which separated on cooling was *N-p*-nitrophenyl-D-xylosylamine, m. p. 191°, $[\alpha]_D^{20}$ +289° (*c*, 0·5 in pyridine). By this method, Weygand, Perkow, and Kuhner (*loc. cit.*) obtained *N-p*-nitrophenyl-D-xylosylamine, m. p. 109°, $[\alpha]_D^{20}$ −95·6° (*c*, 0·5 in pyridine).

(2) A mixture of D-xylose (5 g.), *p*-nitroaniline (5 g.), water (1 ml.), ethanol (5 ml.), and acetic acid (0·1 ml.) was warmed on a steam-bath for 15 min. The ethanol was evaporated and the solid residue, recrystallized from ethanol, washed with ethanol and with ether, and dried in a vacuum-desiccator, was *N-p*-nitrophenyl-D-xylosylamine, m. p. 193°, $[\alpha]_D^{20}$ +294° (*c*, 0·5 in pyridine), for which Weygand *et al.* (*loc. cit.*) record m. p. 192°, $[\alpha]_D^{20}$ +292·5° (*c*, 0·72 in pyridine).

Preparation of N-p-*Nitrophenyl*-D-*ribosylamine.*—By treating D-ribose with *p*-nitroaniline

according to method (1) described for D-xylose there resulted N-p-*nitrophenyl*-D-*ribosylamine* (70%), m. p. 178°, $[\alpha]_D^{20}$ +349° (*c*, 0·4 in pyridine) (Found: C, 48·6; H, 5·2; N, 10·2. $C_{11}H_{14}O_6N_2$ requires C, 48·9; H, 5·2; N, 10·4%).

Mutarotation of N-*Phenyl- and* N-p-*Tolyl*-D-*ribosylamines*.—The specific rotations of each pair, *A* and *B*, were observed in pyridine saturated with hydrogen chloride. With the *N*-*p*-tolyl-D-ribosylamines extensive darkening of the solutions occurred and no further readings were possible after 10 min. but with the *N*-phenyl analogues readings were possible up to an hour after dissolution.

	N-Phenyl-D-ribosylamine			*N*-*p*-Tolyl-D-ribosylamine		
	(1)	(2)		(1)	(2)	
A	+ 178°	→ + 25·7°	→ + 11·3°	+ 163°	→ + 79·5°	→ + 25·9°
B	+ 60	→ + 22·4	→ + 10·9	+ 60·1		→ + 26

(1) = $[\alpha]_D^{20}$ in pyridine. (2) = $[\alpha]_D^{20}$ in pyridine–hydrogen chloride.

General Method for the Preparation of N-*Arylaldosylamine Acetates*.—A solution or suspension of the aldosylamine (5 g.) in acetic anhydride (25 ml.) and pyridine (25 ml.) was left overnight at 0° and then poured into ice and water. The precipitate was stirred until solid, collected, washed with water, and recrystallized from ethanol.

N-*Phenyl*-D-*mannosylamine* 2 : 3 : 4 : 6-*tetra-acetate* had m. p. 127°, $[\alpha]_D^{16}$ −103·1° (*c*, 0·5 in $CHCl_3$) (Found: C, 57·3; H, 5·9; N, 3·4. $C_{20}H_{25}O_9N$ requires C, 56·8; H, 5·9; N, 3·3%).

N-*p*-Tolyl-D-mannosylamine tetra-acetate formed stout prisms, $[\alpha]_D^{20}$ −12·4° (*c*, 1 in $CHCl_3$), m. p. 118—140°, not altered by several recrystallizations from ethanol. An alternative method of preparation gave a similar product.

A solution of D-mannopyranose tetra-acetate (1 g.), m. p. 90—94°, $[\alpha]_D$ +25·8° (*c*, 1 in $CHCl_3$) [prepared by hydrolysis of *N*-*p*-tolyl-D-mannosylamine tetra-acetate], and *p*-toluidine (0·3 g.) in ethanol (10 ml.) was boiled under reflux for 2 hr. and then evaporated at room temperature in the laboratory atmosphere. Large crystals were obtained of *N*-*p*-tolyl-D-mannosylamine 2 : 3 : 4 : 6-tetra-acetate (79%), $[\alpha]_D^{20}$ −16·0° (*c*, 1 in $CHCl_3$), m. p. 120—150°, unaltered when mixed with the above sample (Found: C, 57·7; H, 6·1; N, 3·2. Calc. for $C_{21}H_{27}O_9N$: C, 57·7; H, 6·2; N, 3·2%).

Condensation of p-*Toluidine with* D-*Galactose* 2 : 3 : 4 : 6-*Tetra-acetate*.—Ethanol (10 ml.) containing *p*-toluidine (0·3 g.) and D-galactopyranose tetra-acetate (1 g.) was boiled under reflux for 2 hr. and then evaporated at room temperature in the laboratory atmosphere. The residue, crystallized and recrystallized from ethanol–light petroleum, gave *N*-*p*-tolyl-D-galactosylamine 2 : 3 : 4 : 6-tetra-acetate, m. p. 120—121° (undepressed on admixture with that prepared by the general method), $[\alpha]_D^{19}$ −23·7° (*c*, 1 in $CHCl_3$) (Found: C, 57·9; H, 6·2; N, 3·4. Calc. for $C_{21}H_{27}O_9N$: C, 57·7; H, 6·2; N, 3·2%).

Preparation of N-p-*Nitrophenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—Acetylation of *N*-*p*-nitrophenyl-D-glucosylamine gave the 2 : 3 : 4 : 6-tetra-acetate (88%), m. p. 155°, $[\alpha]_D^{20}$ −95° (*c*, 1 in pyridine). Frèrejacque (*loc. cit.*) records m. p. 155°, $[\alpha]_D^{20}$ −101° (in $CHCl_3$). However, after one recrystallization from ethyl acetate and two from ethanol, the compound had m. p. 179°, $[\alpha]_D^{20}$ −97·8° (*c*, 1 in $CHCl_3$), −120° (*c*, 1 in pyridine), in good agreement with the values recorded by Weygand, Perkow, and Kuhner (*loc. cit.*).

N-p-*Nitrophenyl*-D-*mannosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—Prepared by the standard method in 96% yield this compound had m. p. 186°, $[\alpha]_D^{20}$ −153° (*c*, 1 in $CHCl_3$), −229° (*c*, 1 in pyridine). Frèrejacque (*loc. cit.*) records m. p. 184°, $[\alpha]_D^{20}$ −150° (in $CHCl_3$).

N-p-*Nitrophenyl*-D-*galactosylamine Tetra-acetate*.—This compound, from different preparations, had different melting ranges, starting between 90° and 130°, and continuing to an indefinite upper limit; $[\alpha]_D^{20}$ were −68·3°, −57·8°, and −70·5° for three different preparations (*c*, 1 in chloroform). Frèrejacque (*loc. cit.*) reports $[\alpha]_D^{20}$ −73° (in $CHCl_3$), but does not record the m. p.

N-p-*Nitrophenyl*-D-*xylosylamine* 2 : 3 : 4-*Triacetate*.—Acetylation of *N*-*p*-nitrophenyl-D-xylosylamine gave N-p-*nitrophenyl*-D-*xylosylamine* 2 : 3 : 4-*triacetate* (86%), m. p. 209—211°, $[\alpha]_D^{17}$ −11·5° (*c*, 1 in $CHCl_3$) (Found: C, 51·6; H, 5·2; N, 7·0. $C_{17}H_{20}O_9N_2$ requires C, 51·5; N, 5·1; N, 7·1%).

Hydrolysis of N-*Arylaldosylamine Acetates*.—Aqueous formic acid (80 ml.; 0·5%) was added to a solution of the acetate (2 g.) in acetone (20 ml.), and the mixture was boiled under reflux until homogeneous. *N*-*p*-Tolylaldosylamine acetates were hydrolysed in an atmosphere of

nitrogen to reduce coloration, but this was unnecessary with the *N*-*p*-nitrophenyl analogues. After evaporation of acetone, the sugar acetates were isolated by extraction with chloroform, etc. The products were recrystallized from ether or alcohol. The results are shown in Table 1.

TABLE 1.

Compound hydrolysed : 2 : 3 : 4 : 6-tetra-acetate of	Reaction time (hr.)	Product : 2 : 3 : 4 : 6-tetra-acetate of	Yield (%)	M. p.	$[\alpha]_D$ †	Previous data M. p.	Previous data $[\alpha]_D$ †	Previous data Ref.
N-Phenyl-D-mannosylamine	5	D-Mannose	48	90—94°	+23·5°	93°	+26·3°	1
N-*p*-Tolyl-D-mannosylamine	5	,,	51	90—94	+25·8			
N-*p*-Nitrophenyl-D-mannosylamine	4	,,	56	90—92	+24·7			
N-*p*-Tolyl-D-galactosylamine	5	D-Galactose	50	124—125	+27·5	125—126	+26	2
N-*p*-Nitrophenyl-D-galactosylamine	2	,,	47	124—125	+26·9			
N-*p*-Nitrophenyl-D-glucosylamine	2	D-Glucose	55	123—126 *	+30·8	124—126	+31·6	3
						136—138	+18·8 → +78	4
						120—122	+40	4
						114—117	+46	4
N-*p*-Nitrophenyl-D-xylosylamine 2 : 3 : 4-triacetate	8	D-Xylose 2 : 3 : 4-triacetate	40	132—135 *	−4·5 → +38	136—137	+22·4 → +40·7	5

* Undepressed on admixture with an authentic specimen. † In $CHCl_3$.

References : (1) Levene and Tipson, *J. Biol. Chem.*, 1931, **90**, 89. (2) Butler, Smith, and Stacey, *J.*, 1949, 3371. (3) Ellis and Honeyman, *J.*, 1952, 2053. (4) Hendricks, Wulf, and Liddel, *J. Amer. Chem. Soc.*, 1936, **58**, 1997. (5) Ballou, Roseman, and Link, *ibid.*, 1951, **73**, 1140.

Nitration of N-p-*Tolyl*-β-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—(1) Acetic anhydride (4 ml.) containing fuming nitric acid (1 ml.; 95%) was added to a suspension of *N*-*p*-tolyl-β-D-glucosylamine tetra-acetate (10 g.) in acetic anhydride (15 ml.) at 0°. After an hour at 0° and another hour at room temperature the solution was poured into ice-water. Evaporation of the chloroform extract of this gave a gum which after crystallization and recrystallization from methanol was *N*-(2-nitro-*p*-tolyl)-D-glucosylamine 2 : 3 : 4 : 6-tetra-acetate (2·5 g.), $[\alpha]_D^{18}$ −65·6° (*c*, 1 in $CHCl_3$), m. p. 180—182°, undepressed by a specimen prepared by Mamalis, Petrow, and Sturgeon (*J. Pharm. Pharmacol.*, 1950, **2**, 491).

The yield was doubled by starting the reaction at −70°.

A suspension of this product (5 g.) in glacial acetic acid (5 ml.) was mixed with acetic anhydride (5 ml.) containing fuming nitric acid (1 ml.) at 0°. The yellow precipitate which formed after initial dissolution was dissolved by warming the mixture on a steam-bath for 5 min. After dilution with chloroform (50 ml.) the mixture was poured on ice. Evaporation of the chloroform followed by crystallization and repeated recrystallization of the residue from methanol gave *nitro*-N-(2-*nitro*-p-*tolyl*)-D-*glucosylamine* 2 : 3 : 4 : 6-*tetra-acetate* (5·1 g.), m. p. 157—159°, $[\alpha]_D^{17}$ −51·6° (*c*, 1 in $CHCl_3$) (Found : C, 47·2; H, 4·7; N, 8·1. $C_{21}H_{25}O_{13}N_3$ requires C, 47·8; H, 4·7; N, 8·0%).

(2) Chloroform-soluble nitric acid (50 ml.) was added to a cooled solution of *N*-*p*-tolyl-β-D-glucosylamine 2 : 3 : 4 : 6-tetra-acetate (5 g.) in chloroform (50 ml.) and the solution was stirred at room temperature for 3 hr. The solution gradually changed from deep red to pale yellow. The solution was shaken with water and then with aqueous sodium hydrogen carbonate. Evaporation of the chloroform gave a red syrup, which crystallized from methanol, giving pale yellow crystals of D-*glucosyl*-2 : 6-*dinitro*-N-p-*tolylnitramine* 2 : 3 : 4 : 6-*tetra-acetate* (90%), m. p. 170—171°, $[\alpha]_D^{20}$ −58·4° (*c*, 1 in $CHCl_3$) (Found : C, 44·1; H, 4·3; N, 9·8. $C_{21}H_{24}O_{15}N_4$ requires C, 44·1; H, 4·2; N, 9·8%).

Hydrolysis of N-(2-*Nitro*-p-*tolyl*)- *and of Nitro*-N-(2-*nitro*-p-*tolyl*)-D-*glucosylamine Tetra-acetate*.—Separate solutions of each of these two compounds (1 g.) in acetone (10 ml.) containing aqueous formic acid (40 ml., 0·5%) were boiled under reflux for 3 hr. Evaporation of the acetone yielded 2-nitro-*p*-toluidine (0·26 g.) and 2 : 6-dinitro-*p*-toluidine (0·3 g.), respectively.

Condensation of Acetobromoglucose with 2 : 6-*Dinitro*-p-*tolylnitramine*.—A solution of sodium

hydroxide (0·1 g.) in water (1 ml.) was added to a solution of acetobromoglucose (1 g.) and 2 : 6-dinitro-*p*-tolylnitramine (0·6 g.) in acetone (50 ml.). After 7 days at room temperature, the solution was evaporated at room temperature, to yield crystals of D-glucosyl-2 : 6-dinitro-*p*-tolylnitramine 2 : 3 : 4 : 6-tetra-acetate, m. p. 169° (undepressed on admixture with an authentic specimen prepared as described above), $[\alpha]_D^{20}$ −56·0° (*c*, 1 in $CHCl_3$).

Preparation of Benzoates of N-Arylaldosylamines.—Benzoyl chloride (10 ml.) and pyridine (10 ml.) were added slowly to a solution or suspension of the aldosylamine (5 g.) in pyridine (25 ml.), usually at 0°. After periods ranging from 20 min. to 1 hr., usually at 0°, excess of benzoyl chloride was decomposed by adding drops of ice-water, and the solution was stirred into crushed ice. The precipitate was stirred and, if solid, was collected, washed and recrystallized. In most instances, however, the syrup was extracted with chloroform, and the product isolated by washing and evaporating the chloroform solution. The resulting syrups usually crystallized when triturated with cold alcohol, but for *N*-*p*-nitrophenyl-D-mannosylamine tetrabenzoate and -L-arabinosylamine tribenzoate, and *N*-*p*-tolyl-D-ribosylamine tribenzoate, crystalline products were obtained only after chromatography on alumina with benzene–chloroform (3 : 1 by volume) as solvent and eluant. Recrystallizations were from ethanol–acetone.

Preparation of N-p-*Nitrophenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetrabenzoate.*—(1) Benzoylation of *N*-*p*-nitrophenyl-D-glucosylamine gave, after purification of the chloroform solution, a gum which crystallized when triturated with methanol. Recrystallization gave pure N-p-*nitrophenyl*-β-D-*glucosylamine* 2 : 3 : 4 : 6-*tetrabenzoate* (76%), m. p. 205—207°, $[\alpha]_D^{20}$ −33·3° (*c*, 1 in $CHCl_3$), −4·3° (*c*, 0·7 in pyridine) (Found : C, 67·0; H, 4·4; N, 3·9. $C_{40}H_{32}O_{11}N_2$ requires C, 67·0; H, 4·5; N, 3·9%).

(2) A crude, syrupy tetrabenzoate, obtained by the usual benzoylation procedure, followed by purification of the chloroform solution, was dissolved in acetone–benzene, and the solution was evaporated on a steam-bath until crystallization just began. On cooling, the first crop of crystals (0·2 g.) was collected and recrystallized from ethanol–acetone, yielding N-p-*nitrophenyl*-α-D-*glucosylamine* 2 : 3 : 4 : 6-*tetrabenzoate*, m. p. 246—248°, $[\alpha]_D^{18}$ +166·4° (*c*, 0·7 in pyridine) (Found : C, 66·9; H, 4·5; N, 3·8%). The solubility of this compound in chloroform was unusually low. The main product of the reaction was the β-anomer.

Partial Conversion of N-p-*Nitrophenyl*-β-D-*glucosylamine Tetrabenzoate into its Anomer.*—The β-compound (1 g.) was dissolved at room temperature in a mixture of methanolic hydrogen chloride (25 ml.; 0·1N) and acetone (25 ml.), and left for 20 min. The tetrabenzoate was precipitated by water and recrystallized. The first crop was the α-anomer (0·1 g.), m. p. 246° (undepressed on admixture with a sample prepared as above), $[\alpha]_D^{20}$ +165·0° (*c*, 0·7 in pyridine).

Preparation of N-p-*Nitrophenyl*-D-*mannosylamine* 2 : 3 : 4 : 6-*Tetrabenzoate.*—An amorphous solid was obtained by benzoylation of *N*-*p*-nitrophenyl-D-mannosylamine (1 g.) and subsequent extraction with chloroform. This, purified chromatographically on alumina and crystallized from ethanol–acetone, gave N-p-*nitrophenyl*-D-*mannosylamine* 2 : 3 : 4 : 6-*tetrabenzoate* (92%), m. p. 120°, $[\alpha]_D^{18}$ −124° (*c*, 0·9 in $CHCl_3$) (Found : C, 66·7; H, 4·6; N, 3·9%).

Preparation of N-p-*Tolyl*-D-*ribosylamine* 2 : 3 : 4-*Tribenzoate.*—(1) Benzoyl chloride (10 ml.) in pyridine (10 ml.) was added to a solution of *N*-*p*-tolyl-D-ribosylamine *B* (5 g.) in pyridine (25 ml.) at −70°. The mixture was allowed to attain room temperature during 1 hr., and the product, a red gum, was then isolated. After purification by chromatography the resultant yellow gum was crystallized from ethanol–acetone–light petroleum, followed by recrystallization from aqueous acetone, to give small white needles of N-p-*tolyl*-D-*ribosylamine* 2 : 3 : 4-*tribenzoate* (7·75 g., 64%), m. p. 183—184°, $[\alpha]_D^{17}$ +28·5° (*c*, 1 in $CHCl_3$) (Found : C, 72·1; H, 5·1; N, 2·6. $C_{35}H_{29}O_7N$ requires C, 71·9; H, 5·3; N, 2·5%).

(2) *N*-*p*-Tolyl-D-ribosylamine *A* (2 g.), benzoylated by the procedure used for *B*, gave, after purification in chloroform, a product which crystallized on addition of methanol. After recrystallization from aqueous acetone, the crystals (69%) had m. p. 183—184° (undepressed on admixture with the above tribenzoate), $[\alpha]_D^{19}$ +29·0° (*c*, 1 in chloroform).

Preparation of N-p-*Nitrophenyl*-L-*arabinosylamine* 2 : 3 : 4-*Tribenzoate.*—Benzoylation of *N*-*p*-nitrophenyl-L-arabinosylamine, followed by extraction with chloroform and chromatography, gave from ethanol–acetone, crystals of N-p-*nitrophenyl*-L-*arabinosylamine* 2 : 3 : 4-*tribenzoate* (43%), m. p. 113—116°, $[\alpha]_D^{20}$ +117° (*c*, 0·9 in $CHCl_3$) (Found : C, 66·0; H, 4·6; N, 4·7. $C_{32}H_{28}O_9N_2$ requires C, 66·0; H, 4·5; N, 4·8%).

Preparation of N-p-*Nitrophenyl*-D-*xylosylamine* 2 : 3 : 4-*Tribenzoate.*—Benzoylation of *N*-*p*-nitrophenyl-D-xylosylamine (2 g.) gave N-p-*nitrophenyl*-D-*xylosylamine* 2 : 3 : 4-*tribenzoate* (3·45 g., 80%), m. p. 152—156°, $[\alpha]_D^{19}$ +100° (*c*, 1 in $CHCl_3$) (Found : C, 65·8; H, 4·6; N, 5·0%).

N-p-*Tolyl*-D-*galactosylamine Tetrabenzoate.*—Prepared by the standard method N-p-*tolyl*-D-*galactosylamine tetrabenzoate* had m. p. 190°, $[\alpha]_D$ +101·2° (*c*, 1 in $CHCl_3$) (Found: C, 71·6; H, 5·4; N, 2·3. $C_{41}H_{35}O_9N$ requires C, 71·8; H, 5·2; N, 2·1%).

Benzoylation of N-*Phenyl*-D-*xylosylamine*, N-*Phenyl*-D-*mannosylamine, and* N-p-*nitrophenyl*-D-*ribosylamine.*—When benzoylated these compounds gave syrups.

General Method for Hydrolysis of N-*Arylaldosylamine Benzoates.*—A solution of the *N*-arylaldosylamine benzoate (2 g.) in acetone (100 ml.), water (50 ml.), and concentrated hydrochloric acid (4 ml.) was boiled under reflux during 5 hr. After evaporation of acetone, the sugar benzoate was isolated through extraction with chloroform. D-Glucose tetrabenzoate was recrystallized once from ether and three times from light petroleum (b. p. 100—120°); D-mannose tetrabenzoate and L-arabinose tribenzoate were crystallized from methanol, D-galactose tetrabenzoate from ethanol–light petroleum (attempted recrystallization), and D-ribose tribenzoate from ethanol–water (2 : 1 by vol.).

The results of these hydrolyses are shown in Table 2.

TABLE 2.

Compound hydrolysed	Product	Yield (%)	M. p.	$[\alpha]_D$	Previous data: M. p.	Previous data: $[\alpha]_D$	Previous data: Ref.
N-Phenyl-D-mannosylamine tetrabenzoate	D-Mannose 2 : 3 : 4 : 6-tetrabenzoate	—	181° *	−83·6°	182—184°	−82·6°	1
N-*p*-Nitrophenyl-D-mannosylamine 2 : 3 : 4 : 6-tetrabenzoate	,,	75	180—182 *	−85			
N-*p*-Tolyl-D-galactosylamine tetrabenzoate	Syrup	—	—	—			
N-*p*-Nitrophenyl-β-D-glucosylamine 2 : 3 : 4 : 6-tetrabenzoate	D-Glucose 2 : 3 : 4 : 6-tetrabenzoate	80	117—120 *	+72·4	119—120 114—116	+70·6 † +90·1	2 3
N-Phenyl-D-xylosylamine benzoate	D-Xylose 2 : 3 : 4-tribenzoate	—	180—181 *	+22·5	188—189	+39·5	4
N-*p*-Nitrophenyl-D-xylosylamine 2 : 3 : 4-tribenzoate	,,	67	180—182	+22·2	180—182	→ +23·4 ‡	5
N-*p*-Nitrophenyl-L-arabinosylamine 2 : 3 : 4-tribenzoate	L-Arabinose 2 : 3 : 4-tribenzoate	63	161—163	+241	162—163	+236	6
N-*p*-Tolyl-D-ribosylamine 2 : 3 : 4-tribenzoate	D-Ribose 2 : 3 : 4-tribenzoate	86	130—132 *	−41·1	135—137	−42·2	7
N-*p*-Nitrophenyl-D-ribosylamine 2 : 3 : 4-benzoate	,,	—	130—132	−40·0			

* Denotes undepressed on admixture with an authentic specimen. $[\alpha]_D$ are in $CHCl_3$ unless otherwise stated. † In EtOH. ‡ In dioxan–water (18 : 7) containing a drop of aqueous ammonia.

References: (1) Ness, Fletcher, and Hudson, *J. Amer. Chem. Soc.*, 1950, **72**, 2200. (2) Fischer and Noth, *Ber.*, 1918, **51**, 332. (3) Ellis and Honeyman, *J.*, 1952, 2053. (4) Major and Cook, *J. Amer. Chem. Soc.*, 1936, **58** 2333. (5) Fletcher, *ibid.*, 1953, **75**, 2624. (6) Wolfrom and Christman, *ibid.*, 1936, **58**, 39. (7) Fletcher and Ness, *ibid.*, 1954, **76**, 760.

Preparation of 1-*Deoxy*-O-iso*propylidene*-1-p-*tolylamino*-D-*fructose.*—Concentrated sulphuric acid (4 ml.) was added to a suspension of 1-deoxy-1-*p*-tolylamino-D-fructose (10 g.) [prepared from D-glucose and *p*-toluidine by Weygand's method (*Ber.*, 1940, **73**, 1259)] in acetone (200 ml.), and the mixture was shaken vigorously. The solid dissolved, and after 1 min., the hydrogen sulphate of 1-deoxy-mono-*O*-*iso*propylidene-1-*p*-tolylamino-D-fructose separated, was collected, and, while suspended in acetone (200 ml.), was neutralized by concentrated aqueous ammonia. After the precipitated ammonium sulphate had been collected, the filtrate, evaporated under reduced pressure, yielded crystals (7·4 g., 80%), recrystallization of which from ethanol–light petroleum gave 1-*deoxy*-O-iso*propylidene*-1-p-*tolylamino*-D-*fructose*, m. p. 120—124°, $[\alpha]_D^{19}$ −89·3° (*c*, 1 in EtOH) (Found: C, 62·3; H, 7·6. $C_{16}H_{23}O_5N$ requires C, 62·1; H, 7·4%). This compound was soluble in pyridine, ethanol, and acetone, but sparingly soluble in water, chloroform, and light petroleum.

Hydroxylamine hydrochloride (8 g.) was warmed with a solution of sodium (2·3 g.) in ethanol (100 ml.) until the solution was no longer alkaline. Sodium chloride was filtered off and the resulting solution of hydroxylamine was boiled under reflux with 1-deoxy-*O*-*iso*propylidene-1-*p*-tolylamino-D-fructose (12·4 g.) for 1 hr. On cooling, crystals (10·7 g.), m. p. 122—128°,

separated. Three recrystallizations from ethanol–light petroleum gave 1-*deoxy*iso*propylidene*-1-p-*tolylamino*-D-*fructose oxime*, m. p. 132—134°, $[\alpha]_D^{21}$ −26·6° (*c*, 1 in EtOH) (Found: C, 59·4; H, 7·6; N, 8·6. $C_{16}H_{24}O_5N_2$ requires C, 59·3; H, 7·4; N, 8·6%).

Preparation of O-iso*Propylidene*-D-*glucosazone*.—Phenylhydrazine (2 ml.) and 1-deoxy-*O*-*iso*propylidene-1-*p*-tolylamino-D-fructose (1 g.) were boiled in methanol (40 ml.) and aqueous acetic acid (3 ml.; 50%) for 4 hr. Evaporation of the solvent left a gum which was crystallized, and recrystallized from benzene as yellow crystals of O-iso*propylidene*-D-*glucosazone*, m. p. 186·5—188·5°, $[\alpha]_D^{19}$ +6° (*c*, 0·4 in EtOH) (Found: C, 63·7; H, 6·7; N, 13·9. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5; N, 14·0%).

Periodate Oxidation of 1-*Deoxy*-O-*isopropylidene*-1-p-*tolylamino*-D-*fructose and of* p-*Toluidine*.—Aqueous sodium periodate (60 ml.; *ca.* 0·15M) was added to the fructose derivative (1·0100 g.) dissolved in acetone (20 ml.). The consumption of periodate (mole/mole of derivative) was: after 2·5 hr., 1·92; 5 hr., 2·15; 24 hr., 2·68; 48 hr., 2·80.

With *p*-toluidine (0·3466 g.) in a similar solution the consumption of periodate after 24 hr. was 2·55 mole/mole.

Periodate was estimated by adding excess of standard aqueous sodium arsenite, potassium iodide, and sodium hydrogen carbonate and determining the excess of arsenite after 15 min. with standard iodine solution. Figures given above are corrected for control experiments.

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Some Chlorinated Hydroxyphenoxyacetic Acids.

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The synthesis of 4-chloro-2-hydroxyphenoxyacetic acid, a bacterial metabolite of 4-chlorophenoxyacetic acid, is described; the isomeric 5-chloro-2-hydroxyphenoxyacetic acid has been made from 4-chlorocatechol and by unambiguous synthesis. 3:5-Dichloro-2- and 2:4-dichloro-6-hydroxyphenoxyacetic acid have been prepared by unambiguous routes. The latter is identical with the product prepared by Cavill and Ford (*J.*, 1954, 565) from 3:5-dichlorocatechol. A bacterial metabolite of 2:4-dichlorophenoxyacetic acid is not identical with any of the above acids or with 2-chloro-4-hydroxyphenoxyacetic acid, the synthesis of which is also described.

WHEN this study was commenced, current theories on the fate of 2:4-dichlorophenoxyacetic acid in the plant and in soil substrates favoured *ortho*-hydroxylation to 2:4-dichloro-6-hydroxyphenoxyacetic acid as the initial step. Simultaneously we learned (personal communication) that Professor W. C. Evans had isolated from cultures of bacteria grown on a medium containing 4-chlorophenoxyacetic acid a hydroxy-acid which he believed to be 4-chloro-2-hydroxyphenoxyacetic acid. The preparation of these two possible metabolites for phytotoxicity studies seemed of interest.

2-Amino-4-chlorophenoxyacetic acid which cyclised to the lactam at low pH values was readily obtained by nitration of 4-chlorophenoxyacetic acid and reduction of the product. Attempts to replace the amino-group by hydroxyl in the amino-acid and its derived dimethylamide failed. An unsuccessful attempt was also made to oxidise 2-acetyl-4-chlorophenoxyacetic acid to the required 4-chloro-2-hydroxyphenoxyacetic acid.

Reaction of the monosodium salt of 4-chlorocatechol with ethyl chloroacetate, and subsequent hydrolysis of the product, gave a mixture of acids, which on repeated crystallisation gave 5-chloro-2-hydroxyphenoxyacetic acid. The identity of this acid was established by comparison of its methyl ether with the phenoxyacetic acid from 4-chloroguaiacol (Jona and Pozzi, *Gazzetta*, 1911, **41**, I, 730; cf. Ballio and Almirante, *Ann. Chim. appl.*, 1951, **41**, 421). 5-Chloro-2-hydroxy- and 5-chloro-2-methoxy-phenoxyacetic acid were also prepared from the corresponding 5-nitro-compounds by conventional methods, 4-nitroguaiacol and chloroacetic acid giving either 2-hydroxy- or 2-methoxy-5-nitrophenoxyacetic acid depending on the concentration of alkali employed in the condensation. The required 4-chloro-2-hydroxyphenoxyacetic acid was finally obtained by demethylation of the methoxyacetic acid derived from 5-chloroguaiacol (*idem*, *loc. cit.*). Comparison of this product with the metabolite isolated from cultures of bacteria grown on a medium containing 4-chlorophenoxyacetic acid as the sole source of carbon, showed that the two were identical (Evans and Smith, *Biochem. J.*, 1954, **57**, xxx).

In the preparation of 2 : 4-dichloro-6-hydroxyphenoxyacetic acid we were anticipated by Cavill and Ford (*J.*, 1954, 565) who simply condensed 3 : 5-dichlorocatechol with butyl chloroacetate and hydrolysed the product. In view of our own results with 4-chlorocatechol and ethyl chloroacetate, the success of this method was surprising and, since the diagnostic evidence on which the constitution of the product was based appeared inconclusive, it was decided to prepare samples of 2 : 4-dichloro-6- and 3 : 5-dichloro-2-hydroxyphenoxyacetic acid by unambiguous routes.

Methylation of the *N*-acetyl derivative of the amine obtained by reduction of 2 : 4-dichloro-6-nitrophenol readily gave 2-acetamido-4 : 6-dichloroanisole, which was converted into 4 : 6-dichloroguaiacol and thence into 3 : 5-dichloro-2-hydroxyphenoxyacetic acid by methods similar to those already described. The acid and its methyl ether differed in physical properties from those reported for 2 : 4-dichloro-6-hydroxyphenoxyacetic by Cavill and Ford (*loc. cit.*) and from those of an acid, apparently identical with that prepared by these authors, obtained by condensation of 3 : 5-dichlorocatechol with ethyl chloroacetate.

Oxidation of 2 : 4-dichloroaniline (cf. Boyland, Manson, and Sims, *J.*, 1953, 3623) by potassium persulphate, followed by selective acetylation of the product, gave some of the expected 2-acetamido-3 : 5-dichlorophenol but the yield was so poor that this route was abandoned as a source of 2-amino-3 : 5-dichloroanisole, a precursor of 3 : 5-dichloroguaiacol. It is of interest that methylation of the acetamidophenol led to attack at both the amido- and the hydroxyl group, giving 2-*N*-methylacetamido-3 : 5-dichloroanisole. Decarboxylation of 5-chlorovanillic acid gave 3-chloroguaiacol in low yield but attempts to monochlorinate this material to the required 3 : 5-dichloroguaiacol failed. An alternative approach from 5-chlorovanillic acid was successful. The carboxyl group was replaced by an amino-group by use of the Schmidt reaction, and replacement of the amino-group by chlorine in the normal way gave the required product. 3 : 5-Dichloroguaiacol was also prepared from 2 : 4 : 6-trichloronitrobenzene by way of 3 : 5-dichloro-2-nitroanisole and 2-amino-3 : 5-dichloroanisole. When the *N*-acetyl derivative of this amine was treated with methyl iodide in the presence of potassium carbonate, 2-*N*-methylacetamido-3 : 5-dichloroanisole identical with that obtained previously was formed.

3 : 5-Dichloroguaiacol was converted into 2 : 4-dichloro-6-hydroxyphenoxyacetic acid by the usual sequence of reactions, and the identity of the acid and its methyl ether with the condensation product of 3 : 5-dichlorocatechol and chloroacetic acid and the derived methyl ether confirmed the structures assigned to these products by Cavill and Ford. We have been informed (Professor W. C. Evans, personal communication) that neither 2 : 4-dichloro-6- nor 4-chloro-2-hydroxyphenoxyacetic acid is identical with a compound, believed to be a hydroxy-acid, produced by bacteria growing on a medium containing 2 : 4-dichlorophenoxyacetic acid.

2-Chloro-4-hydroxyphenoxyacetic acid has also been synthesised for comparison with this unknown hydroxy-acid. In a direct approach, 2-chlorophenoxyacetic acid was converted by nitration, esterification, and reduction into methyl 4-amino-2-chlorophenoxyacetate (the orientation of which was checked by replacement of the amino-group with chlorine, followed by hydrolysis). Replacement of the amino- by a hydroxyl group and

subsequent hydrolysis gave 2-chloro-4-hydroxyphenoxyacetic acid identical with the product formed by demethylation of the phenoxyacetic acid from 2-chloro-4-methoxyphenol. This acid also differed in chromatographic behaviour from the 2 : 4-dichlorophenoxyacetic acid metabolite (Professor W. C. Evans, personal communication).

Experimental

4-Chloro-2-nitrophenoxyacetic Acid.—4-Chlorophenoxyacetic acid (10 g.) was heated at 90° for 2 hr. with concentrated nitric acid (100 ml.). The *nitro-acid* separated on cooling in pale yellow needles (7·0 g.), m. p. 170—175°, and recrystallised from aqueous methanol as needles, m. p. 173—175° (Found : C, 42·2; H, 2·4. $C_8H_6O_5NCl$ requires C, 41·6; H, 2·6%).

Reduction of 4-Chloro-2-nitrophenoxyacetic Acid.—The nitro-acid (1·0 g.) was dissolved in 2N-sodium carbonate (10 ml.) and water (10 ml.), and treated at 90° with sodium hyposulphite (dithionite) (2·5 g.) during 10 min. The solution was cooled to 0° and neutralised. No product separated during 1 hr. but on acidification to pH 4 white needles, m. p. 215—218° (0·15 g.), slowly separated. The filtrate was boiled with 32% hydrochloric acid (10 ml.), and more of the same substance (0·52 g.) rapidly separated. This *6-chloro-3 : 4-dihydro-3-oxobenzoxazine* crystallised from ethanol as white needles, m. p. 217—218° (Found : C, 52·9; H, 3·5. $C_8H_6O_2NCl$ requires C, 52·3; H, 3·3%). The lactam (0·6 g.) dissolved in boiling 2N-sodium hydroxide (2 ml.) but was reprecipitated by water (24 ml.).

2-Amino-4-chlorophenoxy-NN-dimethylacetamide.—4-Chloro-2-nitrophenoxyacetic acid (5·0 g.) was boiled with benzene (50 ml.) and thionyl chloride (8·0 ml.) for 8 hr. Benzene and excess of thionyl chloride were evaporated under reduced pressure, and a 20% solution of dimethylamine (4·0 g.) in benzene was added to a solution of the residue in benzene (20 ml.). A yellow precipitate began to separate after 1 hr. After being kept overnight, the mixture was concentrated to 15 ml., cooled, and filtered, and the filtrate was further concentrated to 5 ml. The crude *nitro-amide* (4·7 g.), m. p. 84°, was twice recrystallised from methanol, separating as pale yellow needles, m. p. 100—101° (Found : C, 47·0; H, 4·1. $C_{10}H_{11}O_4N_2Cl$ requires C, 46·4; H, 4·3%). The nitro-amide (3·9 g.) was added in portions during 10 min. to a stirred suspension of iron (9·4 g.) in ethanol (27 ml.), water (47 ml.), and acetic acid (1·9 ml.) at 80°. After 1 hour's heating at 90° the mixture was diluted with hot ethanol (200 ml.) and filtered. The filtrate was concentrated to 30 ml., again filtered at 70° to remove traces of tar, and allowed to cool. The *amino-amide* separated as off-white needles (2·0 g.). Recrystallisation from benzene (5·0 ml.) gave pale buff prisms (1·3 g.), m. p. 117—121°. Concentration of the alcohol and benzene liquors gave less pure product (0·8 g.), m. p. 116—117°. An analytical specimen separated from ethanol as pale cream needles, m. p. 121° (Found : C, 52·4; H, 5·7. $C_{10}H_{13}O_2N_2Cl$ requires C, 52·5; H, 5·7%).

2-Acetyl-4-chlorophenoxyacetic Acid.—5-Chloro-2-hydroxyacetophenone (Auwers and Wittig, *Ber.*, 1924, **57**, 1270) (2·8 g.) was boiled with sodium hydroxide (3·2 g.) and monochloracetic acid (4·7 g.) in water (30 ml.) for 4 hr., with addition of fresh sodium hydroxide (0·3 g.) whenever oil separated. On cooling and acidification, *2-acetyl-4-chlorophenoxyacetic acid* (2·4 g.) was obtained. Recrystallisation from toluene (100 ml.) gave greyish plates (1·8 g.), m. p. 175—178°. An analytical sample was recrystallised from aqueous methanol as greyish-white needles, m. p. 177—178° (Found : C, 52·5; H, 3·9. $C_{10}H_9O_4Cl$ requires C, 52·5; H, 3·9%).

Reaction of 4-Chlorocatechol and Ethyl Chloroacetate.—4-Chlorocatechol (Frejka, Šefránek, and Zika, *Coll. Czech. Chem. Comm.*, 1937, **9**, 238) (14·8 g.) was added to a solution of sodium (2·8 g.) in dry ethanol (60 ml.). To the stirred boiling mixture, ethyl chloroacetate (3·7 g.) in ethanol (40 ml.) was added during 15 min. After boiling for a further 15 min., the solution was kept overnight at room temperature, then poured into water (600 ml.). The oil was extracted with benzene and washed repeatedly with water. The benzene was removed and the product redissolved in ether and shaken with 2N-sodium hydroxide (60 ml.). The mixture became warm and, on acidification of the alkaline layer, impure *5-chloro-2-hydroxyphenoxyacetic acid* (6·4 g.) separated. The crude acid was dissolved in boiling water (75 ml.), then cooled to 40°, and the purified acid (3·0 g.) recovered by filtration. An analytical sample was twice recrystallised from water, forming long, shining colourless needles, m. p. 157°. These were evidently hydrated, losing crystal form on drying at 100° (Found : C, 47·7; H, 3·4; Cl, 17·2. $C_8H_7O_4Cl$ requires C, 47·4; H, 3·5; Cl, 17·5%). The compound gave a blue colour with either aqueous or alcoholic ferric chloride. The acid (0·4 g.) formed a *methyl ether* (0·3 g.), m. p. 137—138°, on treatment

with methyl sulphate and hot 20% aqueous sodium hydroxide. Recrystallisation from aqueous methanol gave pale cream needles, m. p. 143—145° (Found: C, 50·5; H, 4·2. $C_9H_9O_4Cl$ requires C, 49·9; H, 4·2%).

4-Chloroguaiacol.—4-Nitroguaiacol (Paul, *Ber.*, 1906, **39**, 2773) (3·0 g.) in methanol was reduced with hydrogen at room temperature and atmospheric pressure over palladium–charcoal. The reduced compound was filtered into a flask containing excess of methanolic hydrogen chloride. Evaporation of solvent gave 4-aminoguaiacol hydrochloride, which was dissolved in warm 32% hydrochloric acid (30 ml.) and water (10 ml.). The solution was rapidly cooled to 0°, and the resultant slurry diazotised with a solution of sodium nitrite (1·4 g.) in water (5·0 ml.). After destruction of the excess of nitrous acid with urea, a solution of cuprous chloride (from cupric sulphate pentahydrate, 16·6 g.) in 32% hydrochloric acid (30 ml.) was added. After 2 hr. at room temperature and 1 hr. at 90°, the mixture was steam-distilled and 4-chloroguaiacol extracted from the distillate into ether. Evaporation of the dried extract gave a brown oil (1·6 g.) from which the crystalline compound (1·0 g.), m. p. 36—37°, separated at 20°.

5-Chloro-2-methoxyphenoxyacetic Acid.—4-Chloroguaiacol (0·2 g.), chloroacetic acid (0·7 g.), sodium hydroxide (0·5 g.), and water (3·0 ml.) were mixed and heated at 95° for 2 hr. The hot solution was poured into 32% hydrochloric acid (2·0 ml.). An oil (0·2 g.) separated which slowly solidified, and recrystallised from benzene in needles, m. p. 141—143°, undepressed on admixture with the product from 4-chlorocatechol.

Condensation of 4-Nitroguaiacol with Chloroacetic Acid.—(*a*) 4-Nitroguaiacol (1·7 g.), chloroacetic acid (2·9 g.), and sodium hydroxide (2·0 g.) in water (25 ml.) were mixed and the solution boiled for 18 hr. When cloudiness was noticed, sodium hydroxide was added in 0·5-g. amounts. On cooling and acidification, a gelatinous precipitate was obtained which on crystallisation from aqueous methanol (8·0 ml.) formed long, pale cream prisms (0·6 g.), m. p. 191°, of *2-hydroxy-5-nitrophenoxyacetic acid* (Found: C, 44·8; H, 3·3. $C_8H_7O_6N$ requires C, 45·1; H, 3·3%).

(*b*) 4-Nitroguaiacol (8·45 g.), chloroacetic acid (14·2 g.), sodium hydroxide (8 g.), and water (100 ml.) were mixed and the solution boiled for 8 hr. Whenever the solution became cloudy, a drop of 2N-sodium hydroxide was added. After acidification and cooling *2-methoxy-5-nitrophenoxyacetic acid* (9·4 g.), m. p. 180—182°, was obtained. Recrystallisation from aqueous methanol yielded shining, pale yellow prisms, m. p. 182—185° (Found: C, 47·1; H, 4·0. $C_9H_9O_6N$ requires C, 47·6; H, 4·0%).

Conversion of 2-Hydroxy- and 2-Methoxy-5-nitrophenoxyacetic Acids into the 5-Chlorophenoxyacetic Acids.—2-Hydroxy-5-nitrophenoxyacetic acid (0·5 g.) in methanol (50 ml.) was reduced with hydrogen at atmospheric pressure and room temperature with a catalyst from palladium chloride. The amino-acid was rather insoluble in methanol and was removed from the catalyst with alkali. Diazotised and treated with cuprous chloride in the usual way, it furnished crude 5-chloro-2-hydroxyphenoxyacetic acid (0·11 g.), which after recrystallisation from water and from aqueous methanol formed off-white needles, m. p. and mixed m. p. 157° (Found: C, 47·2; H, 3·6. Calc. for $C_8H_7O_4Cl$: C, 47·4; H, 3·5%). Similar treatment of 2-methoxy-5-nitrophenoxyacetic acid gave *5-amino-2-methoxyphenoxyacetic acid* which formed shining buff prisms, m. p. 232°, from water (Found: C, 54·3; H, 5·7. $C_9H_{11}O_4N$ requires C, 54·8; H, 5·6%), and 5-chloro-2-methoxyphenoxyacetic acid (0·39 g. from 0·55 g. of amino-acid) which separated from aqueous methanol in off-white needles, m. p. 140—142°, mixed m. p. 141—143°.

5-Chloroguaiacol.—From 5-nitroguaiacol (Pollecoff and Robinson, *J.*, 1918, **113**, 1647) (4·0 g.), 5-chloroguaiacol (1·2 g.) was obtained by the method described above for 4-chloroguaiacol. This compound has not previously been obtained crystalline but on storage at 0° our sample deposited flaky prisms, m. p. 16—17°.

4-Chloro-2-methoxyphenoxyacetic Acid.—The crude 5-chloroguaiacol (1·5 g.) was treated with chloroacetic acid in the usual way, and the gummy *methoxy-acid* crystallised from benzene, forming needles (0·7 g.), m. p. 135—136°, mixed m. p. with the 5-chloro-2-methoxyphenoxyacetic acid from 4-chlorocatechol, 125—137°. An analytical sample was recrystallised from aqueous methanol (Found: C, 50·1; H, 3·9. $C_9H_9O_4Cl$ requires C, 49·9; H, 4·2%).

4-Chloro-2-hydroxyphenoxyacetic Acid.—4-Chloro-2-methoxyphenoxyacetic acid (0·2 g.) was boiled for 1 hr. with 48% aqueous hydrobromic acid (2·0 ml.). On cooling, the *hydroxy-acid* (0·15 g.) separated. Recrystallisation from water (2 ml.) gave off-white needles (0·1 g.) which lost their sheen at 90° and slowly melted at 110°. The m. p. on rapid heating varied from 124° to 130° (Found: C, 47·0; H, 3·5. $C_8H_7O_4Cl$ requires C, 47·4; H, 3·5%). The substance gave a blue colour with aqueous or alcoholic ferric chloride.

Ethyl 2-Methoxy-4-nitrophenoxyacetate.—5-Nitroguaiacol (2·0 g.) was added to sodium (0·25 g.), dissolved in methanol (20 ml.). Ethyl chloroacetate (1·5 g.) was added and the

mixture boiled for 32 hr. Evaporation of the methanol and boiling of the residue with water (100 ml.) left undissolved oil (0·5 g.) which solidified on cooling, and recrystallised from methanol in pale yellow needles, m. p. 88—91° (Found: C, 51·3; H, 4·9. $C_{11}H_{13}O_6N$ requires C, 51·8; H, 5·1%).

Reaction of **3 : 5-*Dichlorocatechol and Ethyl Chloroacetate.***—**3 : 5**-Dichlorocatechol (3·75 g.), treated with ethyl chloroacetate in the manner described for 4-chlorocatechol, yielded as the least soluble component of the resultant mixture **2 : 4**-dichloro-6-hydroxyphenoxyacetic acid (0·55 g.). An analytical sample was recrystallised from water, forming shining needles which did not lose sheen at 100°. The m. p. varied with the rate of heating between 130° and 155° (Found: C, 41·1; H, 2·8. Calc. for $C_8H_6O_4Cl_2$: C, 40·5; H, 2·6%). The substance gave a cloudy violet solution with aqueous or alcoholic ferric chloride. With methyl sulphate and alkali as described by Cavill and Ford (*loc. cit.*) it formed a methyl ether, m. p. 174—176°.

*2-Acetamido-***4 : 6-*dichlorophenol.***—**2 : 4**-Dichlorophenol (29 g.) was added in small portions to concentrated nitric acid (58 ml.), at 30—40°. On cooling and addition of water (100 ml.), **2 : 4**-dichloro-6-nitrophenol (32·6 g.), m. p. 122—124°, was obtained. The crude nitrophenol (13·7 g.) was dissolved in a solution of sodium carbonate (50 g.) in water (780 ml.) at 90°. Sodium hyposulphite (dithionite) (44 g.) was added during 20 min. The clear, pale yellow solution was neutralised with acetic acid, and the amino-phenol which separated was acetylated by shaking with acetic anhydride (25 ml.) until all solid had liquefied. When kept, the oil solidified and **2-*acetamido*-4 : 6-*dichlorophenol*** (8·0 g.) was recovered by filtration. An analytical sample formed colourless needles, m. p. 138—140°, from aqueous ethanol (Found: C, 43·2; H, 3·2. $C_8H_7O_2NCl_2$ requires C, 43·7; H, 3·2%).

*2-Acetamido-***4 : 6-*dichloroanisole.***—**The crude 2-acetamido-**4 : 6**-dichlorophenol (8·3 g.) was boiled in acetone (50 ml.) with methyl iodide (15 ml.) and potassium carbonate (20 g.) for 6 hr. After evaporation of solvent, water (50 ml.) was added and the oily product extracted into ether. The ***anisole*** separated from the evaporated solution in large plates (4·0 g.) and recrystallised from light petroleum (b. p. 60—80°) in squat white prisms, m. p. 112—114° (Found: C, 45·8; H, 3·5. $C_9H_9O_2NCl_2$ requires C, 46·1; H, 3·8%).

*2-Amino-***4 : 6-*dichloroanisole.***—**2-Acetamido-**4 : 6**-dichloroanisole (3·8 g.) was boiled with 20% hydrochloric acid (150 ml.) for 1 hr. On cooling, **2-*amino*-4 : 6-*dichloroanisole hydrochloride*** separated in white needles, m. p. 196° (previous softening) (from dilute hydrochloric acid) (Found: C, 36·7; H, 3·6. $C_9H_{10}O_2NCl_3$ requires C, 36·7; H, 3·5%). The remainder of the hydrochloride was converted into the amine by addition of sodium hydroxide. The amine was isolated as a brown oil (2·8 g.), f. p. 16°, by extraction into ether.

4 : 6-*Dichloroguaiacol.*—**2**-Amino-**4 : 6**-dichloroanisole (6·1 g.) in concentrated sulphuric acid (38 ml.) was diazotised by addition of sodium nitrite (2·8 g.) at 5°. After 3 hr. the dark solution was poured on ice (100 g.), and the clear diazonium solution was then slowly added to cupric sulphate pentahydrate (100 g.) in water (100 ml.), with simultaneous passage of steam. From the steam-distillate the products were extracted into ether, and purified by dissolution in, and precipitation from, 2N-sodium hydroxide. The light-brown oil (3·3 g.) deposited colourless crystals of **4 : 6-*dichloroguaiacol*** (1·7 g.), needles, m. p. 63—64° [from light petroleum (b. p. 60—80°)] (Found: C, 43·6; H, 3·2. $C_7H_6O_2Cl_2$ requires C, 43·5; H, 3·1%). This compound gave with aqueous ferric chloride a violet colour which was destroyed by addition of alcohol.

3 : 5-*Dichloro-2-hydroxyphenoxyacetic Acid.*—**4 : 6**-Dichloroguaiacol (0·5 g.) was converted in the usual way into **3 : 5-*dichloro-2-methoxyphenoxyacetic acid*** (0·5 g.), white needles, m. p. 106—107° (from toluene) (Found: C, 43·7; H, 3·3. $C_9H_8O_4Cl_2$ requires C, 43·0; H, 3·2%). This methoxy-acid (0·2 g.) was boiled with 48% hydrobromic acid (2·0 ml.) for 1 hr. On cooling, the ***hydroxy-acid*** (0·12 g.) separated. It formed colourless needles, m. p. 154° (from water), which lost their sheen at 100° (Found: C, 40·4; H, 2·6. $C_8H_6O_4Cl_2$ requires C, 40·5; H, 2·6%). The substance gives a royal-blue colour with aqueous or alcoholic ferric chloride.

*2-Acetamido-***3 : 5-*dichlorophenol.***—**2 : 4**-Dichloroaniline (12 g.), dissolved in a mixture of acetone (450 ml.) and water (700 ml.), containing potassium hydroxide (11 g.), was treated during 5 hr. at 25° with a solution of potassium persulphate (20 g.) in water (450 ml.). Next morning potassium hydroxide (1·0 g.) was added, and the liquors concentrated to 250 ml. under reduced pressure. The solution was neutralised, extracted with ether to remove neutral impurities, and then evaporated to dryness (steam-bath). Boiling alcohol (3 × 100 ml.) extracted crystals (1·5 g.) from the residue. These were boiled with 20% hydrochloric acid (3·0 ml.) for 1 hr. The resultant solution was basified with sodium hydrogen carbonate, and acetic anhydride (0·5 ml.) was added to the resultant suspension of 2-amino-**3 : 5**-dichlorophenol.

The *acetamidophenol* (0·4 g.) crystallised from aqueous methanol in cream-coloured plates, m. p. 190—193° (Found: C, 43·5; H, 3·2. $C_9H_7O_2NCl_2$ requires C, 43·7; H, 3·2%).

2-*N*-*Methylacetamido*-3 : 5-*dichloroanisole*.—The foregoing acetamidophenol (0·3 g.), methyl iodide (0·7 g.), potassium carbonate (1·4 g.), and acetone (1·5 ml.) were heated under reflux for 6 hr. The solvent was removed, water (3 ml.) added, and the *methylamide* crystallised from light petroleum (b. p. 60—80°) or aqueous methanol in squat prisms, m. p. 107—109° (Found: C, 48·7; H, 4·7. $C_{10}H_{11}ONCl_2$ requires C, 48·4; H, 4·4%).

3-*Chloroguaiacol*.—5-Chlorovanillic acid (Raiford and Potter, *J. Amer. Chem. Soc.*, 1933, **55**, 1683) (9·0 g.) in glycerol (90 ml.) containing copper bronze (0·2 g.) was heated at 250—260° for 10 min. Steam was passed through the mixture, and 3-*chloroguaiacol* (1·7 g.) was recovered from the distillate by filtration and by ether-extraction. It formed colourless needles, m. p. 54°, from light petroleum (b. p. 60—80°) (Found: C, 52·9; H, 4·2. $C_7H_7O_2Cl$ requires C, 53·0; H, 4·4%). The aqueous solution of the compound gave with ferric chloride a red colour and then a reddish-brown precipitate. A benzene solution of the compound did not react with sulphuryl chloride at room temperature. Boiling it with a large excess of sulphuryl chloride gave a mixed product from which a *trichloroguaiacol*, colourless needles, m. p. 102—104° [from light petroleum (b. p. 60—80°)], was isolated in 5% yield (Found: C, 39·5; H, 2·5. $C_7H_5O_2Cl_3$ requires C, 39·7; H, 2·5%). This substance gave no colour with aqueous or alcoholic ferric chloride. 3-Chloroguaiacol formed a *phenoxyacetic acid* in the usual way in 82% yield (off-white needles, m. p. 130°, from toluene) (Found: C, 50·3; H, 4·3. $C_9H_9O_4Cl$ requires C, 49·9; H, 4·2%).

3 : 5-*Dichloroguaiacol*.—(*a*) 5-Chlorovanillic acid (5·0 g.) was dissolved in warm concentrated sulphuric acid (30 ml.), chloroform (50 ml.) was added, and the mixture stirred at 45° while sodium azide (2·5 g.) was added during 30 min. After 30 min. at 45° the mixture was poured on ice (100 g.), and a trace of unchanged acid removed by filtration. If the mixture is basified with sodium carbonate at this stage, a rapidly discolouring precipitate of 5-amino-3-chloroguaiacol is obtained which can be converted by addition of acetic anhydride into crude 5-*acetamido*-3-*chloroguaiacol* (3·0 g.). A sample of the latter formed pink leaflets, m. p. 165°, from water (Found: C, 49·6; H, 4·9. $C_9H_{10}O_3NCl$ requires C, 50·1; H, 4·7%). To obtain 3 : 5-dichloroguaiacol, the mixture was treated with barium chloride dihydrate (135 g.) in hot water (400 ml.), and the barium sulphate filtered from the amine hydrochloride solution. The latter was diazotised at 5° with sodium nitrite (2·0 g.), kept for 15 min., and treated with urea (1·0 g.) and a solution of cupric chloride from cupric sulphate pentahydrate (83 g.) in hydrochloric acid. This mixture was kept overnight at 20°, heated at 95° for 30 min., and finally steam-distilled. From the distillate (250 ml.) a brown oil (0·5 g.) was extracted with ether, and distilled at 15 mm. (bath-temp. 170°). The pale orange distillate (0·3 g.) partially solidified and was recrystallised three times from light petroleum (b. p. 60—80°), to give 3 : 5-*dichloroguaiacol* as pale yellow needles, m. p. 64—65° (Found: C, 43·7; H, 3·2. $C_7H_6O_2Cl_2$ requires C, 43·5; H, 3·1%). The compound gave no colour with aqueous or alcoholic ferric chloride.

(*b*) 2 : 4 : 6-Trichloronitrobenzene (Loudon, *J.*, 1940, 1527) was condensed with sodium methoxide in boiling methanol as described by Holleman and van Haeften (*loc. cit.*). The crude product, m. p. 41—63°, gave pale yellow cubes of 3 : 5-dichloro-6-nitroanisole, m. p. 70—72° (Found: C, 37·8; H, 2·1; N, 6·2. Calc. for $C_7H_5O_3NCl_2$: C, 37·9; H, 2·3; N, 6·3%), in 40% yield on three recrystallisations from ethanol. Rapid cooling of the hot ethanol solutions gave needles which reverted to the cubic form during several hours. The dichloronitroanisole (3·7 g.) in ethanol (75 ml.) was shaken with hydrogen at atmospheric temperature and pressure in the presence of Raney nickel (1·5 g.) for 24 hr. Evaporation of the filtered solution, finally *in vacuo*, gave 2-amino-3 : 5-dichloroanisole (3·2 g.) as a dark oil. With acetic anhydride it gave 2-*acetamido*-3 : 5-*dichloroanisole*, colourless needles, m. p. 169·5—171·5° (from toluene) (Found: C, 46·2; H, 4·2; N, 5·5; Cl, 30·0. $C_9H_9O_2NCl_2$ requires C, 46·2; H, 3·9; N, 6·0; Cl, 30·3%), and reaction of the amide in acetone with methyl iodide and potassium carbonate gave 2-*N*-methylacetamido-3 : 5-dichloroanisole, m. p. and mixed m. p. 107—109°. 2-Amino-3 : 5-dichloroanisole (3·7 g.) in concentrated sulphuric acid (20 ml.) was converted into 3 : 5-dichloroguaiacol as described in the diazotisation of 2-amino-4 : 6-dichloroanisole. The crude product (0·4 g.), a pale yellow oil, crystallised from light petroleum (b. p. 60—80°) in clusters of pale yellow needles, m. p. and mixed m. p. with sample from (*a*) 60—62·5°.

2 : 4-*Dichloro*-6-*hydroxyphenoxyacetic Acid*.—3 : 5-Dichloroguaiacol (0·6 g.) yielded 2 : 4-dichloro-6-methoxyphenoxyacetic acid (0·7 g.) in the usual way. After two recrystallisations from toluene it formed pale cream-coloured needles, m. p. 174—175°, not depressed on admixture with the methoxy-acid from 3 : 5-dichlorocatechol (Found: C, 42·9; H, 3·7. Calc. for $C_9H_8O_4Cl_2$:

C, 43·0; H, 3·2%). This methoxy-acid (0·2 g.) was boiled under reflux with 48% hydrobromic acid (6 ml.) for 3 hr. Some **3 : 5**-dichloroguaiacol was formed and solidified in the condenser. After cooling, the solid (0·15 g.) was filtered off and boiled with water (3 ml.). The insoluble unchanged methoxy-acid was removed by filtration and **2 : 4**-dichloro-**6**-hydroxyphenoxyacetic acid (0·05 g.) separated from the cool filtrate. It recrystallised from water in needles, the m. p. varying between 135° and 155° according to the rate of heating (Found : C, 41·0; H, 2·8. Calc. for $C_8H_6O_4Cl_2$: C, 40·5; H, 2·6%). The substance gave a cloudy violet colour with aqueous or alcholic ferric chloride.

2-Chloro-4-hydroxyphenoxyacetic Acid (with Ann M. Salaman and J. R. Surtees).—(*a*) 2-Chlorophenoxyacetic acid (12·5 g.) was boiled with concentrated nitric acid (60 ml.) for 5 min., water (50 ml.) was added, and the mixture cooled. *2-Chloro-4-nitrophenoxyacetic acid* (10 g.) separated as plates, m. p. 178—181°. A specimen recrystallised from aqueous ethanol in pale yellow prisms, m. p. 179—181° (Found : C, 42·2; H, 2·8. $C_8H_6O_5NCl$ requires C, 41·6; H, 2·6%). Esterification of the acid (12·5 g.) with methanol and concentrated sulphuric acid gave the methyl ester (10·5 g.) as pale yellow prisms, m. p. 124°. Hydrogenation of the ester in methanol over a palladium catalyst at room temperature and ordinary pressure produced *methyl 4-amino-2-chlorophenoxyacetate*, white needles, m. p. 69° [from a large volume of petroleum ether (b. p. 60—80°)] (Found : C, 50·0; H, 4·5. $C_9H_{10}O_3NCl$ requires C, 50·1; H, 4·6%). The amino-ester (1·0 g.), in water (20 ml.) and concentrated sulphuric acid (2·0 ml.), was diazotised in the usual manner and added dropwise to a boiling solution of cupric sulphate pentahydrate (20 g.) in water (20 ml.). The product was isolated in ether, dissolved in boiling aqueous sodium hydroxide, reprecipitated with acid, dried, and treated with boiling benzene (5·0 ml.). The fraction (0·5 g.) insoluble in benzene was recrystallised twice from water, to give sand-coloured prisms of *2-chloro-4-hydroxyphenoxyacetic acid* (0·1 g.), m. p. 146—147° (Found : C, 46·9; H, 3·1. $C_8H_7O_4Cl$ requires C, 47·4; H, 3·5%). The *methyl ether* formed off-white prisms, 136—138°, from toluene (Found : C, 50·4; H, 4·6. Calc. for $C_9H_9O_4Cl$: C, 49·9; H, 4·2%).

2 : 4-Dichlorophenoxyacetic acid (0·12 g.), m. p. 138—139°, identical with an authentic specimen, was obtained by treatment of the diazonium solution from the above amino-ester (0·6 g.) with cuprous chloride in the usual way.

(*b*) To a stirred solution of *p*-methoxyphenol (30 g.), in chloroform (75 ml.), was added dropwise, during 3 hr., sulphuryl chloride (20 ml.) in chloroform (25 ml.). After 20 hr., solvent was removed and the product distilled. The colourless distillate, b. p. 108°/15 mm., soon solidified. It recrystallised from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 46—47° (Found : C, 52·5; H, 4·5; Cl, 22·5. $C_7H_7O_2Cl$ requires C, 53·0; H, 4·4; Cl, 22·3%) (cf. Nametkin, Bokarev, and Melnikov, *Doklady Akad. Nauk S.S.S.R.*, 1951, **77**, 293, who obtained a liquid, b. p. 97—103°/40 mm., when chlorine was used in this chlorination). This phenol (2·0 g.) formed a phenoxyacetic acid (2·4 g.) in the usual way. A sample, recrystallised from toluene, formed white prisms, m. p. 139°, undepressed on admixture with the above 2-chloro-4-methoxyphenoxyacetic acid. The methyl ether (0·3 g.) was boiled with 48% hydrobromic acid (2·5 ml.) for 1 hr. On cooling, the hydroxy-acid (0·13 g.) separated and formed off-white prisms, m. p. and mixed m. p. 146—147°, from water (Found : C, 47·0; H, 3·6. Calc. for $C_8H_7O_4Cl$: C, 47·4; H, 3·5%).

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Oxygen Heterocycles. Part III. The Reactivity of Benzofuran and 2-Alkylbenzofurans.*

By M. Bisagni, Ng. Ph. Buu-Hoï, and R. Royer.

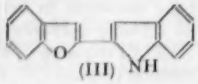
[Reprint Order No. 6472.]

Benzofuran is shown to be more reactive than thionaphthen, and to undergo formylation in position 2; the same reaction occurs at position 3 with 2-substituted coumarones. Benzofuran itself was unstable under the conditions of Friedel–Crafts reactions, but its 2-substituted homologues were readily acylated at position 3. Several cases of steric hindrance were observed, and many new derivatives were prepared.

Whilst the relative reactivities benzene < thiophen < furan have been well established by numerous chemical investigations, and upheld by π-electron-density studies, little comparative experimental or theoretical work has been done with the binuclear sequence naphthalene–thionaphthen (I)–benzofuran (II). A study in this direction has now been undertaken. The reactions used included formylation by means of *N*-methylformanilide

(I)

(II)


(III)

(or dimethylformamide), and Friedel–Crafts acylation with acid chlorides in the presence of stannic chloride. The first of these reactions is known not to give an aldehyde from naphthalene, and gives only very poor yields of 3-formylthionaphthen (cf. Weston and Michaels, *J. Amer. Chem. Soc.*, 1950, **72**, 1422, who recorded a 9% yield; we confirmed this, and failed to improve it with dimethylformamide or *N*-methylformanilide).

Benzofuran has now been found to undergo formylation more easily than thionaphthen, and, unlike the latter, at position 2 (this aldehyde is known; Reichstein *et al.*, *Helv. Chim. Acta*, 1930, **13**, 1275; Normant, *Bull. Soc. chim. France*, 1946, **12**, 609). 2-Methyl- and 2-ethyl-benzofuran (prepared by Wolff–Kishner reduction of 2-formyl- and 2-acetyl-benzofuran) were formylated even more easily, giving excellent yields of 3-formyl-2-methyl- and 2-ethyl-2-formyl-benzofuran; the benzene ring is inert in this reaction, for 2:3-dimethyl- and 2-ethyl-3-methyl-benzofuran are not formylated. A 5-chlorine atom hinders formylation; and a 7-methoxy-group facilitates it.

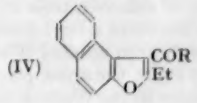
The various formylbenzofurans investigated displayed the normal aldehyde properties (formation of hydrazones, semicarbazones, and oximes), but a 2-alkyl substituent caused steric hindrance, as shown by the increasing difficulty in Wolff–Kishner reduction of the following sequence: 2-formyl-, 3-formyl-2-methyl-, and 2-ethyl-3-formyl-benzofuran; also, the oxime of 2-ethyl-3-formylbenzofuran was readily dehydrated to 3-cyano-2-ethyl-coumarone, but this compound could not be hydrolysed further than to the amide (for similar observations in hydrolysis of amides, see Buu-Hoï and Cagniant, *Compt. rend.*, 1944, **219**, 455; *Rec. Trav. chim.*, 1946, **65**, 246). Further, 2-formyl- but not 2-ethyl-3-formyl-benzofuran gave a chalkone with acetophenone.

The relative reactivities in formylation are found also in Friedel–Crafts acylation. Benzofuran itself is almost wholly resinified by Lewis acids as mild as stannic chloride and phosphoric acid, but 2-alkylbenzofurans are readily acylated at position 3 by acid chlorides in the presence of stannic chloride. Again, 2:3-dialkyl derivatives were unreactive, a 5-chlorine atom hampered the acylation and a 7-methoxy-group favoured it. Propionyl and *n*-butyryl chloride gave similar results.

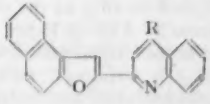
* Papers by Buu-Hoï, *J.*, 1952, 489, and Buu-Hoï and Demerseman, *J.*, 1952, 4699, are considered as Parts I and II of this series.

2-Acetylbenzofuran reacted normally with methylmagnesium iodide to give 2-2′-benzofurylpropan-2-ol, with phenylhydrazine to give a hydrazone which was readily converted by zinc chloride into 2-2′-benzofurylindole (III), and with isatin to give 2-2′-benzofurylcinchoninic acid in excellent yield. 2-Acetyl-5-chloro- and 2-acetyl-7-methoxybenzofuran gave similar cinchoninic acids; and from the three acids the corresponding quinolines were readily prepared by thermal decarboxylation. With 3-acetyl-2-ethylbenzofuran and its 5-chloro- and 7-methoxy-derivatives, however, no Pfitzinger reaction took place, on account of steric hindrance; 2-acetyl-3-ethylthionaphthen is similarly inert (Buu-Hoï and Cagniant, *Ber.*, 1943, **76**, 1269). Steric hindrance would also account for the unusual stability of the hydrazone of 3-acetyl-2-ethylbenzofuran, and the consequent failure to convert it into the 2 : 3-diethyl compound by heating it with potassium hydroxide. It is worth mention that the methyl group of the acetyl radical in 3-acetyl-2-ethylbenzofuran is less subject to steric hindrance, and consequently a chalkone could be prepared with benzaldehyde, and 2-ethylbenzofuran-3-carboxylic acid was obtained by sodium hypobromite degradation.

The naphtho(2′ : 1′-2 : 3)furan nucleus proved chemically similar to coumarone itself, except that its reactivity was less pronounced. Thus, the 5-ethyl derivative, prepared by Wolff–Kishner reduction of the acetyl compound, was formylated to 5-ethyl-4-formylnaphtho(2′ : 1′-2 : 3)furan (IV; R = H) and acylated to the 4-acetyl-5-ethyl analogue



(IV)



(V)

(IV; R = Me), with moderate yields in both cases. Here again, no Pfitzinger reaction occurred with isatin and the ketone (IV; R = Me), whereas 5-acetylnaphtho(2′ : 1′-2 : 3)furan readily gave the cinchoninic acid (V; R = CO_2H), which was decarboxylated to the quinoline (V; R = H).

During this work, Stoermer and Schaeffer's synthesis of 2-acylbenzofuran from ω-halogenated ketones and salicylaldehyde (*Ber.*, 1903, **36**, 2864) was more thoroughly investigated and it was found that the relatively low yields recorded were due to formation of chalkones. Thus, after reaction of chloroacetone with salicylaldehyde, substantial amounts of 2-2′-hydroxycinnamoylbenzofuran were isolated; and there were similar by-products in the reaction with 5-chloro- and 3-methoxy-salicylaldehyde.

Experimental

Formylation of Benzofuran.—Benzofuran was prepared in 29% yield by heating *o*-formylphenoxyacetic acid with acetic anhydride and sodium acetate for 3 hr. (Rössing, *Ber.*, 1884, **17**, 300); the yield was 15·2% when sodium acetate was omitted, and benzofuran-2-carboxylic acid, m. p. 191° (from water), was isolated as a by-product.

To a mixture of benzofuran (46 g.) and dimethylformamide (33 g.), phosphorus oxychloride (66 g.) was added in small portions; heat was evolved, and the mixture was then refluxed for 6—7 hr. with frequent shaking. After cooling, saturated aqueous sodium hydroxide (500 c.c.) was added, the mixture shaken for 15 min., the product taken up in ether, and the ethereal solution washed successively with dilute hydrochloric acid, dilute aqueous sodium carbonate, and water, then dried (Na_2SO_4). The residue from evaporation of the solvent was fractionated *in vacuo*, giving 40% of unchanged benzofuran and 37·7% of 2-formylcoumarone, b. p. 135°/18 mm., $n_D^{22\cdot5}$ 1·6337 [semicarbazone, m. p. 251°; phenylhydrazone, m. p. 136° (lit., m. p. 245—246° and 136—138° respectively)]. β-2-*Benzofurylacrylophenone*, prepared by adding 2 drops of 20% aqueous sodium hydroxide to a solution of 2-formylbenzofuran (1·7 g.) and acetophenone (1·7 g.) in warm ethanol, formed lemon-yellow needles, m. p. 92°, from methanol (Found: C, 81·9; H, 4·7. $C_{17}H_{12}O_2$ requires C, 82·2; H, 4·8%).

2-*Methylbenzofuran.*—A solution of 2-formylbenzofuran (21·5 g.) and 85% hydrazine hydrate (10 g.) in diethylene glycol (100 c.c.) was heated for a few minutes, potassium hydroxide (11·2 g.)

was added, and the mixture refluxed for 2 hr. with removal of both water and the product. The distillate was extracted with benzene, and the benzene layer washed with dilute hydrochloric acid, then with water, and dried (Na_2SO_4). Fractionation of the residue after evaporation of the solvent gave colourless 2-methylbenzofuran (5 g.), b. p. 189—191°.

3-Formyl-2-methylbenzofuran.—2-Methylbenzofuran (5 g.), dimethylformamide (3 g.), and phosphorus oxychloride (6·5 g.) were refluxed for 11 hr. and worked up in the usual way. The *aldehyde* (4·5 g.) formed pale yellow needles, m. p 79°, from light petroleum (b. p. 35—60°) (Found: C, 75·2; H, 5·2. $C_{10}H_8O_2$ requires C, 75·0; H, 5·0%). The *semicarbazone* crystallised as yellowish prisms, m. p. 243° (decomp. above 222°), from ethanol (Found: N, 19·0. $C_{11}H_{11}O_2N_3$ requires N, 19·3%).

2 : 3-Dimethylbenzofuran.—Prepared in 50% yield by Wolff–Kishner reduction of the foregoing aldehyde, this compound was a colourless oil, b. p. 100—101°/15 mm., n_D^{22} 1·5591 (Found: C, 82·2; H, 6·5. $C_{10}H_{10}O$ requires C, 82·1; H, 6·8%); it failed to react with dimethylformamide and phosphorus oxychloride, or with acetyl chloride in the presence of stannic chloride.

Stoermer–Schaeffer Synthesis of 2-Acetylbenzofuran.—In accordance with these authors, a 63% yield was obtained of 2-acetylcoumarone, b. p. 140—145°/15 mm., m. p. 75—76° (from methanol); *2-2′-hydroxycinnamoylbenzofuran*, isolated as a by-product (from the alkaline liquors), crystallised as fine, pale yellow needles, m. p. 193° (decomp. above 177°), from benzene or ethanol, soluble in aqueous sodium hydroxide, and giving a blood red halochromy in sulphuric acid (Found: C, 77·0; H, 4·5. $C_{17}H_{12}O_3$ requires C, 77·3; H, 4·5%). The yield of this compound increased from 5 to 15% as the period of heating of chloroacetone with salicylaldehyde was lengthened from 3—4 hr. to 18 hr., or when a large excess of salicylaldehyde was used. *2-Acetylbenzofuran hydrazone* formed yellow leaflets, m. p. 146°, from ethanol (Found: C, 68·8; H, 5·7; N, 15·8. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·7; N, 16·0%); the *azine*, prepared from the hydrazone and 2-acetylbenzofuran, and isolated as a by-product in the Wolff–Kishner reduction of 2-acetylbenzofuran, formed yellow needles, m. p. 167° (Found: C, 75·7; H, 5·1; N, 8·6 $C_{20}H_{16}O_2N_2$ requires C, 75·9; H, 5·0; N, 8·8%).

2-Ethylbenzofuran.—A solution of 2-acetylbenzofuran (100 g.) and 85% hydrazine hydrate (100 g.) in diethylene glycol (250 c.c.) was brought to the boil, and, after cooling, treated with potassium hydroxide (90 g.), and the mixture was refluxed for 2 hr. with removal of water. After the usual treatment, 2-ethylbenzofuran (83 g., 91%) was obtained as a colourless oil, b. p. 211—212°, n_D^{25} 1·5522; Schreiner and Anderson (*J. Amer. Chem. Soc.*, 1939, **61**, 2705) prepared this compound in another way.

2-2′-Benzofurylcinchoninic Acid.—A solution of 2-acetylbenzofuran (1·6 g.), isatin (1·5 g.), and potassium hydroxide (1·7 g.) in ethanol (10 c.c.) was refluxed for 8 hr. After addition of water and removal of neutral impurities with ether, the aqueous layer gave on acidification with acetic acid the *cinchoninic acid* (90%) which crystallised as pale yellow prisms, m. p. 285—286° (decomp. above 274°), from acetic acid (Found: C, 74·5; H, 3·7; N, 4·6. $C_{18}H_{11}O_3N$ requires C, 74·7; H, 3·8; N, 4·8%). *2-2′-Benzofurylquinoline*, obtained by heating this acid above its m. p. and distilling the residue *in vacuo*, formed colourless needles, m. p. 128°, from ethanol (Found: C, 83·5; H, 4·6; N, 5·5. $C_{17}H_{11}ON$ requires C, 83·2; H, 4·4; N, 5·7%), giving a picrate (yellow needles, from ethanol), m. p. 227° (decomp. above 195°).

2-2′-Benzofurylindole (III).—A solution of 2-acetylbenzofuran (12 g.) and phenylhydrazine (10 g.) in ethanol was refluxed for 10 min. The oil formed on addition of water was taken up in benzene, and the crude solid phenylhydrazone heated with fused zinc chloride (20 g.) at 150—200° for 15 min. After cooling, 10% aqueous sodium hydroxide was added, and the *indole* taken up in benzene and purified by distillation *in vacuo* (b. p. 250—260°/15 mm.). It crystallised as colourless, sublimable prisms, m. p. 218°, from ethanol (Found: C, 82·8; H, 5·0; N, 5·8. $C_{16}H_{11}ON$ requires C, 82·4; H, 4·7; N, 6·0%).

2-2′-Benzofurylpropan-2-ol.—To a cooled ethereal solution of methylmagnesium iodide (prepared from 10 g. of methyl iodide and 2·2 g. of magnesium), 2-acetylbenzofuran (10 g., dissolved in ether) was added dropwise with stirring, and the mixture refluxed for 30 min. After cooling, an ice-cooled solution of ammonium chloride was added, the organic layer washed with water and dried (Na_2SO_4), the solvent evaporated, and the residue fractionated *in vacuo*. The alcohol was a pale yellow oil with a slight aniseed odour, b. p. 138°/15 mm., $n_D^{12\cdot5}$ 1·5783 (Found: C, 75·2; H, 6·6. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%).

2-Ethyl-3-formylbenzofuran.—2-Ethylbenzofuran (30 g.) and dimethylformamide (16·5 g.) were refluxed with phosphorus oxychloride (34·6 g.) for 11 hr., and the product worked up in the usual way. The *aldehyde* (23·5 g.) was a pale yellow oil, b. p. 148—150°/15 mm., $n_D^{22\cdot5}$ 1·5813

(Found : C, 75·5; H, 5·6. $C_{11}H_{10}O_2$ requires C, 75·8; H, 5·7%), giving a cherry-red halochromy in sulphuric acid. The *oxime* formed colourless prisms, m. p. 78°, from ligroin (Found : C, 70·0; H, 5·8; N, 7·5. $C_{11}H_{11}O_2N$ requires C, 69·8; H, 5·8; N, 7·3%).

3-Cyano-2-ethylbenzofuran.—A solution of the foregoing oxime (14 g.) in acetic anhydride (40 g.) was refluxed for 2 hr., and the product fractionated *in vacuo*; the *nitrile* (8·5 g.) was a pale yellow oil, b. p. 149—150°/18 mm., n_D^{23} 1·5596 (Found : C, 77·0; H, 5·3; N, 8·0. $C_{11}H_9ON$ requires C, 77·1; H, 5·3; N, 8·1%). A mixture of this nitrile (3 g.), sulphuric acid (5 c.c.), and water (7 c.c.) was refluxed for 3 hr. After cooling, water was added, and the solid precipitate which formed was recrystallised from water, giving *2-ethylbenzofuran-3-carboxyamide* as colourless needles, m. p. 163—164° (Found : C, 69·6; H, 5·7; N, 7·1. $C_{11}H_{11}O_2N$ requires C, 69·8; H, 5·8; N, 7·4%); no acid was obtained, even on prolonged heating with potassium hydroxide in ethanol.

2-Ethyl-3-methylbenzofuran.—Wolff–Kishner–Huang-Minlon reduction of 2-ethyl-3-formylbenzofuran (10 g.) with hydrazine hydrate (10 g.) and potassium hydroxide (10 g.) in diethylene glycol gave only a 38% yield (3·5 g.) of this *compound*, as a colourless oil, b. p. 108—110°/15 mm., n_D^{24} 1·5611 (Found : C, 82·4; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%). *2-Ethyl-3-formylbenzofuran hydrazone* was recovered unchanged (60% yield), b. p. 220—221°/14 mm., and formed colourless needles, m. p. 136°, from ethanol (Found : N, 14·7. $C_{11}H_{12}ON_2$ requires N, 14·8%).

3-Acetyl-2-ethylbenzofuran.—To a water-cooled solution of 2-ethylbenzofuran (29 g.) and acetyl chloride (16 g.) in dry carbon disulphide (200 c.c.), stannic chloride (52 g.) was added in small portions with stirring, and the mixture left for 3 hr. at room temperature, then poured into water. The organic layer was washed with water and dried (Na_2SO_4), the solvent evaporated, and the residue fractionated *in vacuo*; *3-acetyl-2-ethylbenzofuran* (30 g.; 80·6%) was a yellow oil, b. p. 165—166°/20 mm., n_D^{27} 1·5679 (Found : 76·5; H, 6·7. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). The *oxime*, b. p. 194—195°/20 mm., formed needles, m. p. 81°, from ligroin (Found : C, 70·8; H, 6·4; N, 6·7. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·4; N, 6·8%), and the *thiosemicarbazone* prisms, m. p. 148°, from ethanol (Found : C, 59·6; H, 5·7. $C_{12}H_{15}ON_3S$ requires C, 59·7; H, 5·7%).

Several attempts to reduce this ketone (10 g.) by hydrazine in the usual way led only to the *hydrazone* (8 g.), b. p. 225°/15 mm., prisms, m. p. 121° (from ligroin–*cyclo*hexane) (Found : C, 72·1; H, 7·0; N, 13·7. $C_{12}H_{14}ON_2$ requires C, 71·2; H, 6·9; N, 13·8%).

3-Cinnamoyl-2-ethylbenzofuran.—To a solution of 3-acetyl-2-ethylbenzofuran (3 g.) and benzaldehyde (2 g.) in ethanol, 2 drops of 20% aqueous sodium hydroxide were added, and the mixture was kept at 50° for 15 min. An oil was precipitated, which became solid in the refrigerator, and on recrystallisation from aqueous ethanol gave yellow prisms which changed to a cloudy resin above 93° and a clear liquid at 140° (Found : C, 82·2; H, 5·6. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·7%); sulphuric acid gave an intense red halochromy.

2-Ethylbenzofuran-3-carboxylic Acid.—3-Acetyl-2 ethylbenzofuran (15 g.) was shaken for 2 hr. with aqueous sodium hypobromite (from 27 g. of sodium hydroxide and 13·6 c.c. of bromine in 160 c.c. of ice-cooled water). After addition of sodium hydrogen sulphite, the aqueous layer was acidified with hydrochloric acid, and the *acid* obtained was crystallised from aqueous ethanol, giving prisms (2·5 g.), m. p. 116° (Found : C, 69·8; H, 4·9. $C_{11}H_{10}O_3$ requires C, 69·4; H, 5·2%).

2-Ethyl-3-propionylbenzofuran.—To a solution of 2-ethylbenzofuran (10 g.) and propionyl chloride (6·5 g.) in carbon disulphide (75 c.c.), stannic chloride (18 g.) was added in small portions, and the mixture kept for 18 hr. at room temperature, then worked up in the usual way. The *ketone* obtained (10·3 g.) was a pale yellow oil, b. p. 163—164°/17 mm., n_D^{24} 1·5650 (Found : C, 77·0; H, 7·0. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%). The *oxime* formed needles, m. p. 93°, from ligroin (Found : C, 71·5; H, 6·8. $C_{13}H_{15}O_2N$ requires C, 71·8; H, 6·9%).

3-n-Butyryl-2-ethylbenzofuran.—Prepared as above from 2-ethylbenzofuran (10·5 g.) and *n*-butyryl chloride (8 g.) in 70% yield, this *ketone*, b. p. 178°/20 mm., formed colourless prisms, m. p. 63°, from ligroin (Found : C, 77·6; H, 7·4. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%).

5-Chloro-2-ethylbenzofuran.—2-Acetyl 5-chlorobenzofuran, b. p. 175°/12 mm., m. p. 103°, was prepared in 60% yield from 5-chlorosalicylaldehyde (110 g.) and chloroacetone (69 g.) according to Stoermer (*Annalen*, 1900, **312**, 333); *5 chloro-2-(5-chloro-2-hydroxycinnamoyl)-benzofuran*, obtained as a by-product, formed yellow needles, m. p. 222° (decomp. above 190°), from ligroin (Found : C, 61·5; H, 3·1. $C_{17}H_{10}O_3Cl_2$ requires C, 61·2; H, 3·0%). Reduction of 2-acetyl-5-chlorobenzofuran (33 g.) with hydrazine hydrate (30 g.) and potassium hydroxide (30 g.) in diethylene glycol (150 g.) gave *5-chloro-2-ethylbenzofuran* (25 g.), b. p. 128—129°/15

mm., n_D^{19} 1·5709, having a pronounced aniseed odour (Found: C, 66·1; H, 4·7. $C_{10}H_9OCl$ requires C, 66·4; H, 4·9%).

Formylation of 5-Chloro-2-ethylbenzofuran.—Reaction of 5-chloro-2-ethylbenzofuran (12 g.) with dimethylformamide (6 g.) and phosphorus oxychloride (13 g.), performed as for 2-ethylbenzofuran, gave a 6% yield of 5-chloro-2-formylbenzofuran, b. p. 175°/15 mm., characterised by its *oxime*, needles, m. p. 98° (from light petroleum) (Found: C, 59·3; H, 4·4; N, 6·2. $C_{11}H_{10}O_2NCl$ requires C, 59·0; H, 4·4; N, 6·2%).

2-(5-*Chloro*-2-*benzofuryl*)*cinchoninic Acid.*—Prepared as for the non-chlorinated compound, this *acid* formed from acetic acid yellow needles, m. p. >310° (Found: C, 66·5; H, 3·1. $C_{18}H_{10}O_3NCl$ requires C, 66·8; H, 3·1%); 2-(5-*chloro*-2-*benzofuryl*)*quinoline* crystallised as cream-coloured leaflets, m. p. 189°, from aqueous ethanol (Found: N, 4·9. $C_{17}H_{10}ONCl$ requires N, 4·9%), and its picrate, m. p. 218—219° (decomp. above 190°), formed yellow needles from ethanol.

3-*Acetyl*-5-*chloro*-2-*ethylbenzofuran.*—Prepared from 5-chloro-2-ethylbenzofuran (9 g.), acetyl chloride (6 g.), and stannic chloride (16 g.) in carbon disulphide (80 c.c.) (3 hr. at room temperature), this *ketone* (3 g., 27%), b. p. 170°/13 mm., formed colourless needles, m. p. 59°, from light petroleum (Found: C, 64·8; H, 5·0. $C_{12}H_{11}O_2Cl$ requires C, 64·7; H, 4·9%); it gave a yellow halochromy with sulphuric acid.

2-*Acetyl*-7-*methoxybenzofuran.*—Prepared from *o*-vanillin (100 g.), chloroacetone (66·5 g.), and potassium hydroxide (38 g.) in ethanol, this *ketone* (58 g.), b. p. 176—180°/15 mm., formed colourless needles, m. p. 94°, from water, giving an orange halochromy with sulphuric acid (Found: C, 69·4; H, 5·3. $C_{11}H_{10}O_3$ requires C, 69·4; H, 5·2%). Reduction of this ketone (22 g.) with hydrazine hydrate (22 g.) and potassium hydroxide (20 g.) in diethylene glycol (100 c.c.) afforded 2-*ethyl*-7-*methoxybenzofuran* (16·5 g., 81%) as a pale yellow oil, b. p. 136—137°/13 mm., $n_D^{22·5}$ 1·5610 (Found: C, 74·8; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%).

2-(7-*Methoxy*-2-*benzofuryl*)*cinchoninic acid* crystallised as pale yellow needles, m. p. 282°, from acetic acid (Found: C, 71·2; H, 4·0. $C_{19}H_{13}O_4N$ requires C, 71·5; H, 4·1%); 2-(7-*methoxy*-2-*benzofuryl*)*quinoline* formed pale yellow leaflets, m. p. 148°, from ligroin (Found: C, 78·1; H, 4·8; N, 4·9. $C_{18}H_{13}O_2N$ requires C, 78·5; H, 4·7; N, 5·1%), and gave a picrate, golden-yellow needles, m. p. 220° (decomp. above 192°), from ethanol.

2-*Ethyl*-3-*formyl*-7-*methoxybenzofuran.*—This *aldehyde* (7 g., 76%), prepared from 2-ethyl-7-methoxybenzofuran (8 g.), dimethylformamide (4 g.), and phosphorus oxycbloride (8·3 g.), formed colourless needles, m. p. 62°, from light petroleum (Found: C, 70·8; H, 6·0. $C_{12}H_{12}O_3$ requires C, 70·5; H, 5·8%) and gave a yellow halochromy with sulphuric acid and a *semicarbazone*, prisms (from aqueous ethanol), m. p. 174° (Found: N, 15·8. $C_{13}H_{15}O_3N_3$ requires N, 16·0%).

3-*Acetyl*-2-*ethyl*-7-*methoxybenzofuran.*—Prepared from 2-ethyl-7-methoxybenzofuran (3 g.), acetyl chloride (2 g.), and stannic chloride (6 g.) in carbon disulphide (50 c.c.) (15 min. at room temperature), this *ketone* (2 g., 54%) formed prisms, m. p. 57°, from light petroleum (Found: C, 71·6; H, 6·5. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·4%); it gave a yellow colour in sulphuric acid.

5-*Ethylnaphtho*(2′ : 1′-2 : 3)*furan.*—5-Acetylnaphtho(2′ : 1′-2 : 3)furan, b. p. 245°/15 mm., m. p. 114° (from ligroin), was prepared according to Stoermer and Schaeffer (*loc. cit.*); the 2-hydroxy-1-naphthaldehyde used was obtained by Fosse's method (*Bull. Soc. chim. France*, 1901, 25, 373; Buu-Hoï, Hiong-Ki-Wei, and Royer, *Compt. rend.*, 1945, 220, 361). The ketone (29 g.) with hydrazine hydrate (15 g.) and potassium hydroxide (15 g.) in diethylene glycol (120 c.c.) afforded the 2-*ethyl derivative* (22 g., 81·4%) as a pale yellow, viscous oil, b. p. 180—185°/15 mm., n_D^{23} 1·6388, giving an orange halochromy with sulphuric acid (Found: C, 85·8; H, 6·5. $C_{14}H_{12}O$ requires C, 85·7; H, 6·1%).

Pfitzinger reaction of the ketone (5 g.) with isatin (5·6 g.) afforded 2-(4-*carboxy*-2-*quinolyl*)-*naphtho*(2′ : 1′-2 : 3)*furan* (V; R = CO_2H) which was purified through its sparingly soluble sodium salt, and formed yellowish needles, m. p. >330°, from acetic acid (Found: C, 77·6; H, 3·6. $C_{22}H_{13}O_3N$ requires C, 77·9; H, 3·8%). The 2-2′-*quinolyl derivative* (V; R = H) formed yellow prisms, m. p. 159°, from ligroin (Found: C, 85·5; H, 4·4; N, 4·4. $C_{21}H_{13}ON$ requires C, 85·4; H, 4·4; N, 4·7%), and gave a picrate, fine orange needles (from ethanol), decomp. >210°.

5-*Ethyl*-4-*formylnaphtho*(2′ : 1′-2 : 3)*furan* (IV; R = H).—This *aldehyde* (4·6 g., 49·5%), prepared from the 2-ethyl compound (8 g.), dimethylformamide (3·1 g.), and phosphorus oxychloride (6·5 g.) in toluene (50 c.c.), formed cream-coloured needles, m. p. 79°, b. p. 240—245°/20 mm., from light petroleum (Found: C, 80·4; H, 5·4. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·3%), giving a greenish-yellow halochromy with sulphuric acid and a *semicarbazone*, fine, pale yellow

leaflets, m. p. 258° (decomp. >234°), from ethanol (Found: N, 14·8. $C_{16}H_{15}O_2N_3$ requires N, 14·9%).

4-*Acetyl-5-ethylnaphtho*(2′ : 1′-2 : 3)*furan* (IV; R = Me).—This *ketone* (3 g., 32·6%), prepared from the 2-ethyl compound (8 g.), acetyl chloride (3·3 g.), and stannic chloride (11 g.) in carbon disulphide (100 c.c.), formed pale yellow prisms, m. p. 70°, b. p. 245—250°/15 mm., from light petroleum (Found: C, 80·6; H, 5·9 $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·8%).

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*Oxygen Heterocycles. Part IV.** 2-Benzoylbenzofurans and Related Compounds with Biological Interest.

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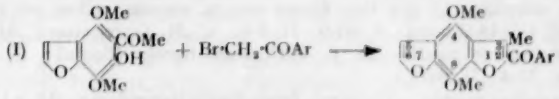
[Reprint Order No. 6492.]

The chemistry of 2-aroylbenzofurans and their derivatives has been investigated, and some of the compounds showed œstrogenic activity. The Rap–Stoermer benzofuran cyclisation was successfully extended to *o*-hydroxy-ketones, including khellinone (5-acetyl-6-hydroxy-4 : 7-dimethoxybenzofuran), and several 2-aroyl-4 : 7-dimethoxy-3-methylbenzo[1 : 2-*b*, 4 : 5-*b*]difurans were prepared.

RECENTLY, natural and synthetic œstrogenic substances have been found in oxygen-heterocyclic compounds such as some *iso*flavones, *iso*flavens (Bradbury and White, *J.*, 1951, 3447; 1953, 871), and coumarins (Gley and Mentzer, *Compt. rend. Soc. Biol.*, 1945, **139**, 1055). The similarity between these and benzofuran derivatives suggested the investigation of 2-aroylbenzofurans and related compounds. 2-Benzoylbenzofuran was prepared by Rap (*Gazzetta*, 1895, **25**, II, 285) by the reaction of ω-bromoacetophenone with the sodio-derivative of salicylaldehyde, and this procedure was now successfully extended to substituted derivatives of each. Further, it was found that in the Rap reaction *o*-hydroxyaldehydes could be replaced by *o*-hydroxy-ketones; *o*-hydroxypropiophenone thus gave 2-benzoyl-3-ethyl- and 2-*p*-anisoyl-3-ethyl-benzofuran with ω-bromo- and ω-bromo-4-methoxy-acetophenone respectively. Khellinone (I) (Späth and Gruber, *Ber.*, 1938, **71**, 106; Schönberg and Sina, *J. Amer. Chem. Soc.*, 1950, **72**, 1611, 3396) readily gave



2-benzoyl-4 : 8-dimethoxy-3-methylbenzo[1 : 2-*b*, 5 : 4-*b*]difuran (II; R = Ph) with ω-bromoacetophenone, and similar derivatives were obtained with aryl-ω-bromo-ketones. On the other hand, *o*-hydroxy-ketones could not be used in the similar Stoermer synthesis of 2-acetylbenzofurans from chloroacetone (Stoermer, *Annalen*, 1900, **312**, 333; Stoermer and Schaeffer, *Ber.*, 1903, **36**, 2864), thus indicating that the methylene group in phenacyl ethers RO·CH_2·COAr is more reactive than in acetonyl ethers RO·CH_2·COMe.

2-*p*-Hydroxybenzoyl- and 3-ethyl-2-*p*-hydroxybenzoyl-benzofuran and 2-benzoyl-6-hydroxybenzofuran were readily obtained by demethylation of the corresponding methyl ethers with pyridine hydrochloride. Similar ketones with the aroyl group in position 3 (cf. preceding paper) included 3-benzoyl-2-ethyl-, 2-ethyl-3-*p*-toluoyl-, and 2-ethyl-3-phenylacetyl-benzofuran. Wolff–Kishner reduction of 2-benzoylbenzofuran readily afforded the 2-benzyl compound, which likewise underwent acylation, to give 3-acetyl-2-benzylbenzofuran.

The œstrogenic activities of the various benzofuran derivatives, determined in spayed mice by the Allen–Doisy test (subcutaneous injection), are in the Table. These results

* Part III, preceding paper.

stress the importance of a *p*-hydroxy-group in the 2-aroyl substituent, a requirement for œstrogenic activity similar to that observed in the *iso*flavone (Bradbury and White, *loc. cit.*) and the coumarin group.

During this research, a convenient technique for the preparation of 2 : 4-dihydroxybenzaldehyde from resorcinol, dimethylformamide, and phosphorus oxychloride was devised.

Œstrogenic activity of benzofurans

2-*p*-Hydroxybenzoyl	active at 1 mg.
3-Ethyl-2-*p*-hydroxybenzoyl	active between 1 and 10 mg.
2-Benzoyl-6-hydroxy	inactive at 1 mg.
3-Benzoyl-2-ethyl	inactive at 1 mg.
2-*p*-Anisoyl-3-ethyl	inactive at 10 mg.
2-*o*-Hydroxycinnamoyl	inactive at 1 mg.

Experimental

2-Benzylbenzofuran.—2-Benzoylbenzofuran, b. p. 214—216°/15 mm., m. p. 90° (from ethanol), was prepared in 58% yield according to Rap. A solution of this ketone (120 g.) and 85% hydrazine hydrate (110 g.) in diethylene glycol (300 c.c.) was refluxed for 10 min. and, on cooling, treated with potassium hydroxide (100 g.). The mixture was then heated for a further 3 hr. with removal of water, and after cooling it was acidified with dilute hydrochloric acid; the product was taken up in benzene and purified by distillation *in vacuo*. 2-Benzylbenzofuran was a pale yellow oil (77 g., 68% yield), b. p. 184—185°/16 mm., n_D^{20} 1·6056 (Found: C, 86·5; H, 5·9. Calc. for $C_{15}H_{12}O$: C, 86·5; H, 5·7%).

3-Acetyl-2-benzylbenzofuran.—To an ice-cooled solution of 2-benzylbenzofuran (30 g.) and acetyl chloride (13 g.) in dry carbon disulphide (150 c.c.), stannic chloride (40 g.) was added in small portions, and the mixture kept at room temperature for 1 hr. After decomposition with hydrochloric acid, the organic layer was washed with water and dried (Na_2SO_4), the solvent removed, and the residue fractionated *in vacuo*. The *ketone* (13 g.) was a yellow, viscous oil, b. p. 228—230°/18 mm., n_D^{19} 1·6181, giving an orange-red halochromy with sulphuric acid (Found: C, 81·9; H, 5·8. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%). The *oxime* formed colourless leaflets, m. p. 134°, from ligroin (Found: C, 76·9; H, 5·7. $C_{17}H_{15}O_2N$ requires C, 76·9; H, 5·6%).

3-Benzoyl-2-ethylbenzofuran.—This *ketone* (3·5 g.), prepared as above from 2-ethylcoumarone (10 g.), benzoyl chloride (11 g.), and stannic chloride (18 g.; 18 hr. at room temperature), was a yellow oil, b. p. 210°/15 mm., giving a red halochromy in sulphuric acid (Found: C, 81·6; H, 5·8%). The *oxime* formed colourless needles, m. p. 118°, from ligroin (Found: C, 77·2; H, 5·4%).

3-p-Anisoyl-2-ethylbenzofuran.—Prepared from 2-ethylbenzofuran (6·5 g.), *p*-anisoyl chloride (8 g.), and stannic chloride (12 g.), this *ketone* was a viscous yellow oil (4·5 g.), b. p. 225—226°/15 mm., n_D^{23} 1·6249 (Found: C, 81·9; H, 6·4. $C_{18}H_{16}O_3$ requires C, 81·8; H, 6·1%). The *oxime* formed colourless needles, m. p. 161°, from ligroin (Found: C, 77·6; H, 6·0. $C_{18}H_{17}O_3N$ requires C, 77·4; H, 6·0%).

2-Ethyl-3-phenylacetylbenzofuran.—Prepared from 2-ethylbenzofuran (10 g.), phenylacetyl chloride (12 g.), and stannic chloride (16 g.), this *ketone* (11 g.) was a yellow oil, b. p. 232—233°/16 mm., n_D^{20} 1·6138 (Found: C, 82·0; H, 6·2%); the *oxime* formed leaflets, m. p. 117°, from ligroin (Found: C, 77·7; H, 6·3%).

2-Benzoyl-3-ethylbenzofuran.—To a solution of *o*-hydroxypropiophenone (30 g.) and potassium hydroxide (13 g.) in ethanol (150 c.c.), ω-bromoacetophenone (40 g.) was added, and the mixture refluxed for 2½ hr. The oil precipitated on addition of water was taken up in benzene and purified by distillation *in vacuo*. The *ketone* (14 g., 28%) was a pale yellow oil, b. p. 215—218°/15 mm., n_D^{20} 1·6270 (Found: C, 81·3; H, 5·5%). Wolff–Kishner reduction of this ketone (5 g.) with hydrazine hydrate (3 g.) and potassium hydroxide (2 g.) in diethylene glycol (25 c.c.) afforded *2-benzyl-3-ethylbenzofuran* (2·5 g.), a pale yellow oil, b. p. 202—204°/16 mm., n_D^{20} 1·5940 (Found: C, 86·1; H, 6·6. $C_{17}H_{16}O$ requires C, 86·4; H, 6·7%).

2-p-Anisoylbenzofuran.—To a solution of salicylaldehyde (20·5 g.) and potassium hydroxide (10·5 g.) in ethanol (150 c.c.), ω-bromo-4-methoxyacetophenone (38 g.) was added, and the mixture refluxed for 3 hr. The precipitated potassium bromide was filtered off, and the *ketone* which separated from the filtrate on cooling was recrystallised from ethanol, giving colourless leaflets (15 g.), m. p. 97° (Found: C, 76·1; H, 5·0. $C_{16}H_{12}O_3$ requires C, 76·1; H, 4·7%). A mixture of this ketone (10 g.) and redistilled pyridine hydrochloride (20 g.) was refluxed for

40 min., and the precipitate formed on addition of water was recrystallised several times from benzene, giving 2-*p*-hydroxybenxoylbenzofuran, cream-coloured needles (8 g.), m. p. 192—193°, soluble in aqueous alkalis with a yellow colour. Zwayer and Kostanecki (*Ber.*, 1908, **41**, 1332) gave m. p. 179—180°.

2-p-*Anisoyl*-3-*ethylbenzofuran*.—This *ketone*, prepared from *o*-hydroxypropiophenone (45 g.), potassium hydroxide (17 g.), and ω-bromo-4-methoxyacetophenone (65 g.) in ethanol (4 hours' refluxing), was a yellow oil (23 g.), b. p. 245—247°/17 mm., n_D^{21} 1·6447, which crystallised (Found: C, 76·9; H, 5·8. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%). Demethylation of this ketone (12 g.) with pyridine hydrochloride (20 g.) as above, yielded 3-*ethyl*-2-p-*hydroxybenzoylbenzofuran* (10 g.), yellowish needles, m. p. 167—168° (from benzene) (Found: C, 76·3; H, 5·1. $C_{17}H_{14}O_3$ requires C, 76·6; H, 5·2%).

2 : 4-*Dihydroxybenzaldehyde*.—The following procedure was convenient: to a mixture of resorcinol (220 g.) and dimethylformamide (146 g.), phosphorus oxychloride (153 g.) was added in small portions with stirring, and the mixture kept for 2 hr. at room temperature; the thick magma was treated with a hot 50% aqueous solution of sodium acetate (1500 c.c.) to complete dissolution and, on cooling, the product was taken up in ether; the ethereal layer was washed with water, dried (Na_2SO_4), and evaporated. The residue gave on distillation *in vacuo* 2 : 4-dihydroxybenzaldehyde (125 g.), m. p. 135° (from water).

2-*Benzoyl*-6-*methoxybenzofuran*.—A solution of 2-hydroxy-4-methoxybenzaldehyde (13·5 g.) and potassium hydroxide (5·5 g.) in ethanol was refluxed with ω-bromoacetophenone (18 g.) for 3 hr. After cooling, water was added, and the *ketone* was collected and crystallised from methanol, giving colourless leaflets (11 g.), m. p. 105° (Found: C, 76·3; H, 4·9. $C_{16}H_{12}O_3$ requires C, 76·1; H, 4·7%) (red halochromy in sulphuric acid). 2-*Benzoyl*-6-*hydroxybenzofuran*, prepared by refluxing this ketone (4 g.) and pyridine hydrochloride (8 g.) for 40 min., formed cream-coloured needles, m. p. 215° (from aqueous ethanol) (Found: C, 75·3; H, 4·5. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%), giving yellow solutions in aqueous alkalis.

5-*Acetyl*-4 : 6 : 7-*trimethoxybenzofuran*.—Khellinone (44 g.) was prepared by refluxing a solution of khellin (50 g.) in 10% aqueous potassium hydroxide (500 c.c.) for 2 hr. After cooling, the insoluble impurities were filtered off, the filtrate acidified with dilute hydrochloric acid, and the yellow precipitate collected and crystallised from aqueous methanol (m. p. 100—101°). A solution of khellinone (16 g.) in 10% aqueous potassium hydroxide (50 g.) was heated with methyl sulphate (11 g.) at 100° for 30 min. After alternate addition of potassium hydroxide and methyl sulphate (5 g.), the mixture was basified, and the precipitated oil taken up in benzene and purified by fractionation *in vacuo*. 5-*Acetyl*-4 : 6 : 7-*trimethoxybenzofuran* (12·5 g.) was a pale yellow oil, b. p. 138—140°/0·1 mm., $n_D^{20\cdot5}$ 1·5542, with an aromatic odour (Found: C, 62·1; H, 5·5. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%).

2-*Benzoyl*-4 : 8-*dimethoxy*-3-*methylbenzo*(1 : 2-b, 5 : 4-b)*difuran* (II; Ar = Ph).—To a solution of khellinone (6 g.) and potassium hydroxide (2 g.) in ethanol (25 c.c.), ω-bromoacetophenone (6 g.) was added, and the mixture refluxed for 18 hr. The precipitate of sodium bromide was filtered off, and the filtrate concentrated; the *benzodifuran* precipitated on cooling gave bright yellow leaflets (4 g.), m. p. 127°, from ligroin or aqueous ethanol (Found: C, 71·1; H, 4·7. $C_{20}H_{16}O_5$ requires C, 71·4; H, 4·7%). The bathochromic effect produced by the introduction of a second furan ring is probably due to the resonance between the two furan rings *via* the benzene nucleus (cf. II).

2-p-*Methylbenzoyl*-4 : 7-*dimethoxy*-3-*methylbenzo*(1 : 2-b, 5 : 4-b)*difuran* (II; Ar = *p*-C_6H_4Me), similarly prepared from ω-bromo-4-methoxyacetophenone (6 g.), khellinone (6 g.), and potassium hydroxide (2 g.), formed yellow needles (4·2 g.), m. p. 124°, from ethanol (Found: C, 71·9; H, 5·2. $C_{21}H_{18}O_5$ requires C, 72·0; H, 5·1%). The 2-p-*ethylbenzoyl analogue* (II; Ar = *p*-C_6H_4Et) formed bright yellow needles, m. p. 118°, from ligroin (Found: C, 72·2; H, 5·6. $C_{22}H_{20}O_5$ requires C, 72·5; H, 5·5%). The 2-p-*Anisoyl analogue* (II; Ar = *p*-C_6H_4OMe) formed yellow needles, m. p. 135°, from ligroin (Found: C, 69·0; H, 5·0. $C_{21}H_{18}O_6$ requires C, 68·9; H, 4·9%).

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Precise Measurements with the Glass Electrode. Part I. The Cell: Glass Electrode|HCl|AgCl|Ag.

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It is shown that glass electrodes are capable of giving results of precision comparable to that of the best results obtained with the hydrogen electrode. The electrodes used were of such low resistance that no amplifier was necessary. The effect of asymmetry potentials was eliminated by a simple procedure. Values obtained for the activity coefficient of hydrochloric acid over the molality range 0·005—0·1 are in good agreement with these reported by Hills and Ives (*J.*, 1951, 305) from their accurate work on the hydrogen–calomel cell.

The introduction of the glass electrode has greatly increased the number of electrolytic solutions which can be studied by e.m.f. cell techniques. Because of the high resistance of the electrodes and the presence of asymmetry potentials, their use for accurate work has been very restricted. Commercial pH meters with electrometer-valve potentiometers are available, but these measure only to ± 1 mv, whereas a precision of about $\pm 0{\cdot}01$ mv has been attained in the best work with the hydrogen electrode (Hills and Ives, *J.*, 1951, 305). A precision of about $\pm 0{\cdot}1$ mv has sometimes been reached by using electrostatic electrometers (see, *e.g.*, MacInnes and Belcher, *J. Amer. Chem. Soc.*, 1933, **55**, 2630; Pedersen, *Kgl. Danske Videnskab. Selskabs*, 1937, **14**, No. 9) or specially constructed valve potentiometers (Greville and MacLagan, *Trans. Faraday Soc.*, 1931, **27**, 210). However, glass electrodes with a resistance as low as 0·5 MΩ are now available, as well as robust moving-coil galvanometers of high sensitivity, and we have made accurate measurements with such equipment employing a conventional potentiometer circuit with no special amplifying devices.

We believe, following Beck and Wynne-Jones (*J. Chim. phys.*, 1952, **49**, C 97), that two distinct potentials must be recognized when a glass electrode is placed in a solution, *viz.*: (1) A potential set up instantaneously which varies with the hydrogen-ion concentration of the solution (the hydrogen-electrode function of the glass electrode); and (2) the so-called asymmetry potential, the e.m.f. of the cell

$$\mathrm{Ag|AgCl|HCl}(m)\mathrm{|glass|HCl}(m)\mathrm{|AgCl|Ag}$$

which is due to differences in the two surfaces of the glass membrane. The e.m.f. changes with time and probably depends on the exchange of ions or water between the solution and the glass.

It is usual in work with glass electrodes to make one measurement of asymmetry potential suffice for a series of measurements on test solutions. The precision of our measurements, however, revealed that the e.m.f. of a cell was slowly changing (Fig. 4) and we have therefore used a procedure in which this effect is taken into account. By a simple extrapolation procedure we obtain values of the e.m.f. E_A and E_B that the cells A and B

$$\underline{\mathrm{Ag|AgCl|HCl}(m_1')}\mathrm{|glass|HCl}(m_1)\mathrm{|AgCl|Ag} \quad . \quad . \quad . \quad . \quad . \quad \text{(A)}$$

$$\underline{\mathrm{Ag|AgCl|HCl}(m_1')}\mathrm{|glass|HCl}(m_2)\mathrm{|AgCl|Ag} \quad . \quad . \quad . \quad . \quad . \quad \text{(B)}$$

would have at the moment of transfer of the glass electrode from one cell to the other; the asymmetry potential is therefore the same for the two cells. The enclosed part on the left of the cells represents the glass electrode filled with hydrochloric acid and containing an internal silver–silver chloride reference electrode.

If the glass membrane is permeable to hydrogen ions only, we can combine cells A and B to obtain a cell which is thermodynamically equivalent to the cell :

$$Ag|AgCl|HCl(m_1)|Pt,H_2 \ldots\ldots H_2,Pt|HCl(m_2)|AgCl|Ag$$

whose e.m.f. E is given by

$$E = E_B - E_A = -2k \log (m_2\gamma_2) + 2k \log (m_1\gamma_1) \quad . \quad . \quad . \quad . \quad (1)$$

where $k = (RT/F)\ln 10$, and m_1, m_2, and γ_1, γ_2 are the respective molalities and mean ionic activity coefficients of the hydrochloric acid. Since the asymmetry potential makes the same contribution to E_A and E_B, its effect is eliminated. If during a series of measurements cell A is the same, we can regard the electrode assembly as a whole as having a kind of " standard " potential E° and can write

$$E = E^\circ - 2k \log (m_2\gamma_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where

$$E^\circ = 2k \log (m_1\gamma_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

A useful way of representing activity coefficients for uni-univalent electrolytes is (Guggenheim and Prue, *Trans. Faraday Soc.*, 1954, **60**, 231) :

$$\log \gamma = -Am^{\frac{1}{2}}/(1 + m^{\frac{1}{2}}) + Bm \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where A is the Debye–Hückel constant and B an empirical parameter. Substituting in (2) we obtain (dropping the subscript 2) :

$$E^{\circ\prime} = E + 2k \log m - 2kAm^{\frac{1}{2}}/(1 + m^{\frac{1}{2}}) = E^\circ - 2kBm \quad . \quad . \quad . \quad (5)$$

If we plot $E^{\circ\prime}$ against m, we should obtain a straight line with intercept E° and slope $2kB$.

Experimental

Hydrochloric Acid.—" AnalaR " acid was chlorinated and boiled to free it from other halogens. The purified acid was distilled to give a constant-boiling fraction. The concentration of the acid obtained was determined by interpolation from Foulk and Hollingsworth's concentration–pressure data (*J. Amer. Chem. Soc.*, 1923, **45**, 1220).

Solutions were prepared by weight from conductivity water, made by passing laboratory distilled water through a column of mixed ion-exchange resins, De-Acidite F.F. and Zeo-Karb 315 supplied by the Permutit Co.

Electrodes.—The glass electrodes were Type 9000 (blue trademark) of the Jenaer Glaswerk Schott und Gen., Landshut, Bavaria. Their resistance was 0·3—0·6 MΩ, and their bulb diameter 30 mm. They were mounted as shown in Fig. 1. The split rubber bung held the electrode in a larger Polythene stopper. The central hole was tapered to hold the rubber bung and was large enough to pass the neck of the electrode. The gap below the rubber bung, between the Polythene and the stem, was filled with cotton-wool, and the lower surface of the Polythene stopper and the exposed stem were coated with paraffin wax to suppress electrical leakage. With an electrode whose stem was unwaxed, changing the liquid level by 1 cm. caused the measured e.m.f. to change by 0·3 mV, presumably because of electrical leakage along a film of moisture on the stem and on the Polythene. The electrodes were filled with 0·1M-hydrochloric acid and the internal silver–silver chloride electrode was held in place by a Polythene stopper.

The silver–silver chloride electrodes were of the thermal-electrolytic type. These are type 2 as described by Harned (*J. Amer. Chem. Soc.*, 1929, **51**, 416). The electrodes were stored in 0·1M-hydrochloric acid. Some electrodes showed bias potentials (intercomparison e.m.f. in a common electrolyte) as large as 200 μV but in most cases the bias potentials were less than 60 μV after 24 hr. These differences decreased within a few days. The electrodes chosen for use were from a group which showed the smallest bias potentials. It was found possible to reduce still further the bias potentials of the better electrodes by heating them in water at 50° for 2 hr. as described by Ashby, Crook, and Datta (*Biochem. J.*, 1954, **56**, 190). We chose the silver–silver chloride electrode as the external electrode in these cells, although Hills and Ives (*J.*, 1951, 305) have shown, and we have confirmed, that, provided sufficient care is taken, the calomel electrode is more reproducible. The silver–silver chloride electrode is simpler and

quicker to prepare and may conveniently be rejected if showing a large bias potential. It is well known that oxygen affects the silver–silver chloride electrode in acid solution (Smith and Taylor, *J. Res. Nat. Bur. Stand.*, **1939**, **22**, 307), and therefore purified nitrogen was bubbled through the cells before measurements were made. The nitrogen from a commercial cylinder was purified by passage through 5% aqueous potassium hydroxide and an electrically heated silica furnace at 600° packed with alternate sections of reduced copper gauze and filings. Before passing into the electrode vessel (Fig. 2), the gas was presaturated by bubbling through a wash-bottle, immersed in the thermostat, containing hydrochloric acid of the same concentration as that in the vessel. The gas train was of glass, connections being made with ground joints except for two short sections of Polythene tubing to give flexibility. In this Polythene tubing a packing of glass wool allowed the flow of gas to be adjusted by means of screw clips so that the gas could be bubbled through both cells at once.

Circuit.—The potentiometer used was the Tinsley Vernier Potentiometer Type 3126B (1949). The standard cell was checked against a laboratory standard which had been calibrated at the N.P.L. The galvanometer was a Tinsley Type 4500L with a resistance of 400 Ω and a maximum

FIG. 1.

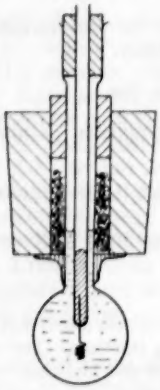
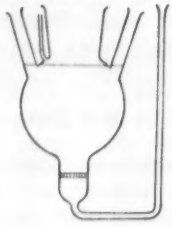


FIG. 2.



sensitivity of 3040 mm./μA. If the smallest detectable deflection on a scale at one metre is 0·1 mm. and the electrodes have a resistance of 0·3 MΩ, we should be able to detect:

$$\Delta E = (0{\cdot}1 \times 0{\cdot}3 \times 10^6 \times 10^{-6}/3040)\ \text{v} \simeq 0{\cdot}01\ \text{mv}$$

We could in fact distinguish a difference in setting of the potentiometer of 0·005 mv.

The galvanometer and potentiometer stood on an " equipotential surface " of copper sheets connected in a series to a common earth (White, " Temperature : Its Measurement and Control in Science and Industry," Reinhold Publ. Corp., New York, 1941, pp. 279—283; see also *J. Amer. Chem. Soc.*, 1914, **36**, 2011). The copper thermostat was also connected to the common earth, as was the shielding of the galvanometer and cell leads. The use of an " equipotential shield " and screened flex for the leads to the galvanometer and cell was found to be essential. Accurate results were not possible without close attention being paid to these details. The electrode vessels were in a thermostat maintained at 25° ± 0·005°. The thermostat thermometer was calibrated against an N.P.L. calibrated thermocouple.

Experimental Procedure.—Two electrode vessels (Fig. 2) were set up in the thermostat containing hydrochloric acid of molalities m_1 and m_2. Two silver–silver chloride electrodes of small bias-potential were inserted, one in each vessel. The cells were left for 1 hr. to come to equilibrium, during the last ½ hr. of which nitrogen was bubbled through the vessels. Meanwhile, the glass electrode was in a jar of distilled water also in the thermostat. The glass electrode was put into the electrode vessel of cell A (see p. 3696) and e.m.f. readings taken every minute for 10 min. The glass electrode was then transferred to the electrode vessel of cell B for 10 min. and then back to A for a further 10 min., e.m.f. readings being taken at 1-min. intervals throughout. Before insertion in an electrode vessel the electrode was washed quickly with some solution of the same molality from a Polythene wash-bottle kept in the thermostat.

While readings were being made on one cell, nitrogen was bubbled through the other. With one filling of the electrode vessels two runs were performed with each of two glass electrodes. The bias potentials of the external silver–silver chloride electrodes were checked before each run and never exceeded 40 μv. No correction was applied for the bias potential.

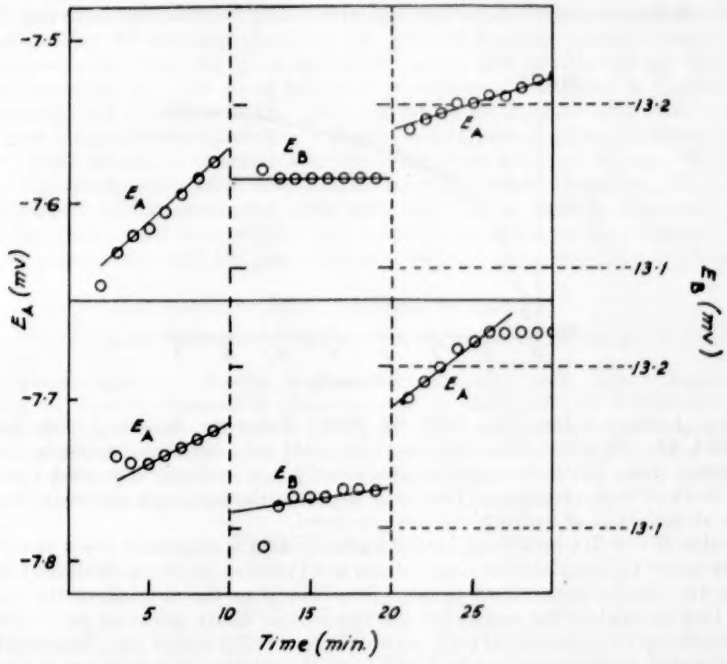
Results and Discussion

A typical set of e.m.f. readings for $m_1 = 0{\cdot}1111$ mole kg.$^{-1}$, $m_2 = 0{\cdot}07222$ mole kg.$^{-1}$ are plotted for one electrode (No. 2) in Fig. 3. In Table 1 singly and doubly primed symbols relate to the extrapolated values at times 10 and 20 min. respectively.

Table 1.

Glass electrode no.	E_A' (mv)	E_B' (mv)	E (mv)	E_A'' (mv)	E_B'' (mv)	E (mv)
1	$-5{\cdot}88_5$	14·91	$20{\cdot}79_5$	−5·87	14·97	20·84
1	−5·87	14·95	20·82	$-5{\cdot}83_5$	14·98	$20{\cdot}81_5$
2	$-7{\cdot}66_5$	$13{\cdot}15_5$	20·82	$-7{\cdot}65_5$	$13{\cdot}15_5$	20·81
2	$-7{\cdot}71_5$	13·11	$20{\cdot}82_5$	$-7{\cdot}70_5$	$13{\cdot}12_5$	20·83

Fig. 3.



The mean value of E is 20·82 mv. We have found that the change of e.m.f. with time due to changing asymmetry potential continues indefinitely as shown for a typical cell in Fig. 4. The asymmetry potentials of the electrodes when used were rather high (6—8 mv); even higher values were obtained when the electrodes were first tested, but these were reduced by storage of the electrodes in hydrochloric acid.

The results obtained are summarized in Table 2, where $m_1 = 0{\cdot}1111$ mole kg.$^{-1}$ throughout. We have used the values $2k = 118{\cdot}318$ mv and $A = 0{\cdot}5084$ kg.$^{\frac{1}{2}}$ mole$^{-\frac{1}{2}}$ based on Birge's list of the fundamental constants (*Reports Progr. Phys.*, 1941, **8**, 90) and the value 78·54 for the dielectric constant of water (Wyman and Ingalls, *Phys. Rev.*, 1930, **35**, 623; *J. Amer. Chem. Soc.*, 1938, **60**, 1182).

If $E^{o\prime}$ is plotted against m_2 a straight line can be drawn from which no point

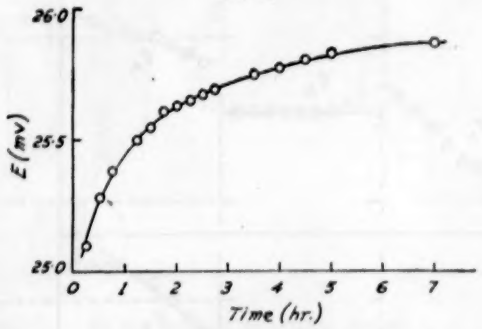
deviates by more than 0·05 mv. The slope of the best straight line obtained by application of the method of least squares is 25·4 ± 0·5 mv mole^{-1} kg., which gives B = 0·214 ± 0·004 mole^{-1} kfl. The value of the intercept is E° = −125·18 mv. Values of $E^{\circ\prime}$

TABLE 2.

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	$-E^{\circ\prime}$ (exp.) (mv)	$-E^{\circ\prime}$ (calc.) (mv)	$E^{\circ\prime}$ (exp.) − $E^{\circ\prime}$ (calc.) (mv)
5·36	147·46	125·32	125·32	0·00
11·59	109·40	125·50	125·48	−0·02
22·57	76·96	125·71	125·75	+0·04
30·04	63·02	125·99	125·94	−0·05
42·32	46·52	126·24	126·23	−0·01
47·90	40·60	126·34	126·39	+0·05
60·79	29·05	126·74	126·76	−0·02
72·22	20·82	126·96	127·00	+0·04
81·14	15·13	127·29	127·24	−0·05

calculated from equation (5) by using these values of B and E° are compared with the experimental values in Table 2. The scatter of the experimental points is a little greater than in the work of Hills and Ives (*loc. cit.*) on the hydrogen–calomel cell, but less than in previous work on cells with the hydrogen and silver–silver chloride electrodes (*e.g.*, Harned

FIG. 4.



and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350; Bates and Bower, *J. Res. Nat. Bur. Stand.*, 1954, **53**, 283) where the scatter is about ±0·1 mv. Our results clearly show that low-resistance glass electrodes can be satisfactorily and conveniently used for electrochemical work of high precision. The deviation from the hydrogen-electrode function is negligible at molalities of hydrochloric acid up to 0·1.

The value B = 0·214 mole^{-1} kg. for hydrochloric acid is somewhat lower than a value B = 0·234 mole^{-1} kg. calculated by Guggenheim and Prue (*loc. cit.*) from the data of Hills and Ives over the same concentration range. However, if in the analysis of the results of Hill and Ives we neglect the results for the three most dilute solutions ($m \ll 0{\cdot}005$) and use the results up to a molality of 0·12, we obtain B = 0·225 mole^{-1} kg. Smoothed values of γ at rounded concentrations calculated from the various B values are compared in Table 3. We emphasize that a difference in B of 0·01 corresponds to a difference in γ of only ¼% at a molality of 0·1.

TABLE 3.

m (mole kg.$^{-1}$)	γ (B = 0·214)	γ (B = 0·225)	γ (B = 0·234)	m (mole kg.$^{-1}$)	γ (B = 0·214)	γ (B = 0·225)	γ (B = 0·234)
0·001	0·9653	0·9653	0·9653	0·02	0·8736	0·8740	0·8744
0·005	0·9279	0·9280	0·9281	0·05	0·8276	0·8285	0·8295
0·01	0·9035	0·9036	0·9039	0·08	0·8036	0·8051	0·8065

Our thanks are offered to the Department of Scientific and Industrial Research for a grant to one of us (A. K. C.) with respect to this and the following paper.

READING UNIVERSITY. [*Received, May 9th*, 1955.]

Precise Measurements with the Glass Electrode. Part II. The Cell: Glass Electrode*|HCl(m_1)|HCl(m_2)|*Glass Electrode.*

By A. K. Covington and J. E. Prue.

[Reprint Order No. 6405.]

It is shown that glass electrodes can be used for precise electrochemical measurements on cells with transport. Values obtained for the activity coefficient of hydrochloric acid are compared with those from other sources.

Concentration cells with two similar electrodes have been widely used in physicochemical studies. For instance, precise activity-coefficient values can be obtained by the combination of e.m.f. measurements on cells with transport-number data obtained by the moving-boundary technique (Brown and MacInnes, *J. Amer. Chem. Soc.*, **1935**, **57**, 1356). Unfortunately, in many cases suitable electrodes are not available. Previously it has been impossible to make satisfactory measurements on cells of the type: glass electrode|Solution **1**|Solution **2**|glass electrode. By a development of the procedure described in Part I * we show that it is now possible to make precise measurements on concentration cells with two glass electrodes, which will greatly extend the range of solutions amenable to exact study by e.m.f. techniques. We report a determination of activity coefficient values for hydrochloric acid which we compare with other exact data. We are now using a similar procedure in studies of solutions of nitric, perchloric, and other oxidizing acids for which no suitable electrode has been available before. We have also repeated Shedlovsky and MacInnes's measurements (*J. Amer. Chem. Soc.*, **1936**, **58**, 1970) on hydrochloric acid concentration cells with silver–silver chloride electrodes, since we suspect that their results were vitiated by a failure to deoxygenate the solutions.

In our experiments with the glass electrode we have measured the e.m.f.'s of pairs of cells:

glass electrode (p)|HCl(m_1)|glass electrode (q) . . . . . (A)

glass electrode (p)|HCl(m_1)|HCl(m_2)|glass electrode (q) . . . (B)

where "glass electrode" denotes a glass electrode filled with hydrochloric acid and containing an internal silver–silver chloride reference electrode. By a time-extrapolation procedure we obtain values of the e.m.f.'s E_A and E_B that the cells A and B would have at the moment of transfer of the glass electrodes from one cell to the other. The sum of the asymmetry potentials, equal to E_A, is therefore the same in the two cells, and the e.m.f. $E = E_B - E_A$ is the e.m.f. of the thermodynamically equivalent cell

$$H_2,Pt|HCl(m_1)|HCl(m_2)|Pt,H_2$$

This e.m.f. is given by

$$E = \frac{2RT}{F}\int_{m_1}^{m_2} t^- \, \mathrm{d} \ln (m\gamma) \quad . . . . . (1)$$

where γ is the mean ionic activity coefficient at molality m and t^- is the value of the transport number of the chloride ion. Expressing t^- in the form $t^- = t_1 + \Delta t$, where t_1 is the transport number of the chloride ion at molality m_1, we obtain

$$\log \frac{\gamma_2}{\gamma_1} = \frac{E}{t_1 RT \ln 10/F} - \log \frac{m_2}{m_1} - \frac{1}{t_1}\int_{m_1}^{m_2} \Delta t \, \mathrm{d} \log m - \frac{1}{t_1}\int_{\gamma_1}^{\gamma_2} \Delta t \, \mathrm{d} \log \gamma \quad . . (2)$$

The value of the third term on the right-hand side of equation (2) is obtained by graphical integration from a plot of Δt against $\log m$. The fourth term is small and is given with sufficient accuracy by graphical integration using values of $\log \gamma$ obtained from equation (2) with this fourth term omitted.

* Part I, preceding paper.

We represent the activity coefficient values as in Part I by the expression

$$\log \gamma = -Am^{\frac{1}{2}}/(1 + m^{\frac{1}{2}}) + Bm \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where A is the Debye–Hückel constant, and B an empirical parameter. Defining a standard value γ^{st} of the activity coefficient by setting $B = 0$ in (3), we obtain $\log \gamma - \log \gamma^{st} = Bm$, and denoting by Δ the difference between values at m_1 and m_2, we have

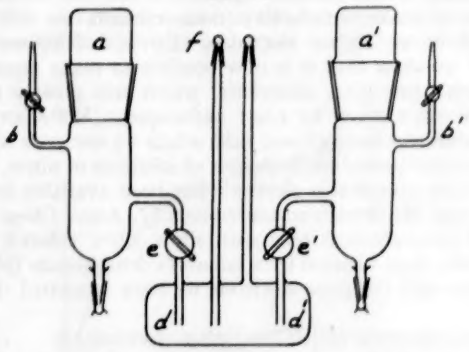
$$\Delta \log \gamma - \Delta \log \gamma^{st} = B\Delta m \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

We therefore plot values of $\Delta \log \gamma - \Delta \log \gamma^{st}$ against Δm to obtain a value for B.

Experimental

Solutions of hydrochloric acid were prepared as in Part I. They were deoxygenated immediately before use by passage of a stream of purified and pre-saturated nitrogen. The electrodes and the electrical circuit were the same as those described in the previous paper.

Fig. 1.



Procedure.—The electrode vessel used is shown in Fig. 1. The taps e,e' were fitted to prevent disturbance of the junction either by removal or insertion of electrodes, or by convection currents due to thermal gradients when the vessel was first placed in the thermostat. The taps were lightly greased with a Silicone grease.

In the filling procedure the stoppers a,a' were held in place by rubber bands and the vessel was inverted. One of the solutions was forced into the left-hand compartment through b until the liquid level had reached the end of tube d. The right-hand compartment was filled similarly with the other solution, after which taps e and e' were closed and the vessel was returned to its original position. The more concentrated of the two solutions was now carefully admitted through f until the central compartment was full. The vessel, supported in a brass frame, was now transferred to the thermostat, taps e,e' being kept closed until temperature equilibrium had been reached. The glass electrodes (stored in distilled water at 25°) were washed with solution of molality m_1 at 25° and placed in the electrode vessel of cell A (see p. 3701) also in the thermostat. Readings of the e.m.f. of cell A were taken every minute for 5 min., the electrodes were transferred (with appropriate washing) to the concentration cell B, and the taps e,e' opened. Readings were again taken at 1-min. intervals for 10 min., the electrodes were transferred back to cell A, and e.m.f. readings taken for a further 5 min. The whole procedure was repeated, the position of the electrodes in cell B being reversed.

Measurements were also made by using silver–silver chloride electrodes. A steady potential with fluctuations of only a few microvolts was reached in 90 min. Electrodes with bias potentials less than 20 μv were chosen. No correction was applied for any residual bias potential but in a series of measurements with increasing m_2 an electrode was used alternately in the dilute or concentrated solution.

Results and Discussion

A typical set of e.m.f. readings with the glass electrode cells with $m_1 = 0{\cdot}1093$ mole kg.$^{-1}$ and $m_2 = 0{\cdot}02118$ mole kg.$^{-1}$ is shown in Fig. 2, and the results of the extrapolations in Table 1. The e.m.f. of the cell with the electrode positions in cell B reversed we denote by

E_C, and therefore $E = E_C + E_A$. Occasionally the two pairs of values of E disagreed and the results were rejected. The mean value of E in this experiment was therefore 13·51 mv. The results obtained are summarized in Table 2. The corresponding results for the silver–silver chloride cell are given in Table 3, and Shedlovsky and MacInnes's results (*loc. cit.*)

TABLE 1.

Time (min.)	E_A (mv)	E_B (mv)	E (mv)	Time (min.)	E_A (mv)	E_C (mv)	E (mv)
5	−5·05	8·46	13·51	20	−5·05	$18·57_5$	$13·52_5$
15	−5·05	$8·44_5$	$13·49_5$	30	−5·00	$18·50_5$	$13·50_5$

recalculated on the molality scale are given in Table 4. In this we have used density values interpolated from Redlich and Bigeleisen's data (*J. Amer. Chem. Soc.*, 1942, **64**, 758) and converted international volts to absolute volts by using the relation 1 int. v = 1·00034 v. In all calculations we have used the value of the fundamental constants given in Part I, and transport-number data interpolated from Longsworth's results (*ibid.*, 1932, **54**, 2741).

The results of the three sets of experimental work are plotted together in Fig. 3, on which is also shown the change in $\Delta \log \gamma - \Delta \log \gamma^{at}$ caused by a change of 0·1 mv in E for

FIG. 2.

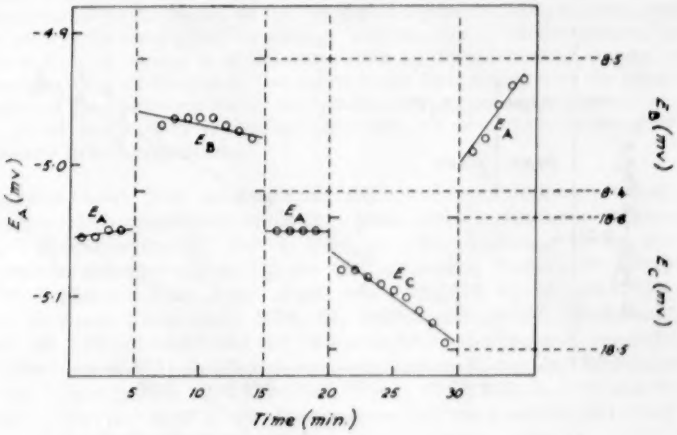


TABLE 2. *Glass electrode results.*

$m_1 = 0·1093$ mole kg.$^{-1}$, $t_1 = 0·1682$.

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	t^-	$-\Delta \log \gamma$	$\frac{\Delta \log \gamma}{-\Delta \log \gamma^{at}}$	Δm
5·930	24·42	0·1761	0·06831	0·02166	0·1034
13·04	17·61	0·1744	0·05499	0·01923	0·0962
21·18	13·51	0·1732	0·04439	0·01734	0·0881
30·03	10·60	0·1722	0·03514	0·01609	0·0792
45·02	7·25	0·1711	0·02441	0·01294	0·0643
49·73	6·42	0·1708	0·02199	0·01163	0·0595
62·40	4·58	0·1702	0·01463	0·01008	0·0469
72·06	3·38	0·1697	0·01188	0·00685	0·0372

TABLE 3. *Silver–silver chloride electrode results.*

$m_1 = 0·1093$ mole kg.$^{-1}$, $t_1 = 0·8318$.

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	t^+	$-\Delta \log \gamma$	$\frac{\Delta \log \gamma}{-\Delta \log \gamma^{at}}$	Δm
5·434	120·85	0·8237	0·06904	0·02238	0·1038
5·930	117·22	0·8239	0·06848	0·02149	0·1034
13·04	85·27	0·8256	0·05360	0·02062	0·0962
21·18	65·73	0·8268	0·04268	0·01905	0·0881
30·03	51·68	0·8978	0·03460	0·01663	0·0792
45·02	35·48	0·8289	0·02424	0·01311	0·0643
49·73	31·53	0·8292	0·02110	0·01252	0·0595
62·40	22·46	0·8298	0·01496	0·00975	0·0469
72·06	16·68	0·8303	0·01129	0·00744	0·0372

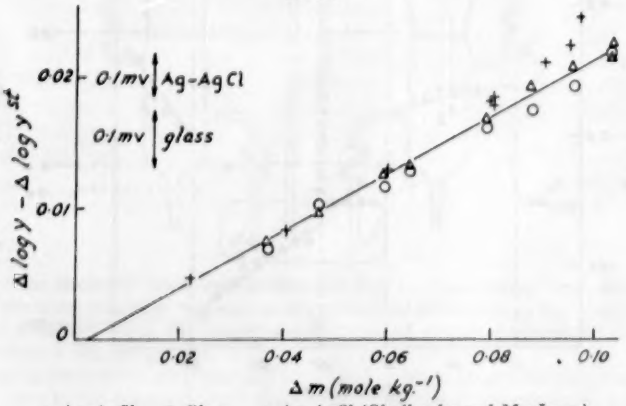
the glass or silver–silver chloride electrode cells. The best straight line through our results with the silver–silver chloride electrode has a slope of $B = 0{\cdot}217$ mole^{-1} kg.; the line does not pass through the origin, but the negative intercept on the ordinate corresponds to an error of only 0·1% in m_1, which is within the accuracy with which we knew the value of m_1. The deviation of the points from the line never exceeds a value corresponding to 0·02 mv,

TABLE 4. *Recalculated results of Shedlovsky and MacInnes.*

$m_1 = 0{\cdot}1048$ mole kg.$^{-1}$, $t_1 = 0{\cdot}8314$.

$10^3 m_2$ (mole kg.$^{-1}$)	E (mv)	t^+	$-\Delta \log \gamma$	$-\Delta \log \gamma^{t_1}$	$\Delta \log \gamma$ Δm
3·457	136·310	0·8234	0·06981	0·02438	0·09702
5·275	118·855	0·8239	0·06541	0·02254	0·09520
10·049	92·560	0·8251	0·05505	0·02100	0·09043
10·061	92·511	0·8251	0·05503	0·02100	0·09042
19·980	64·752	0·8266	0·04124	0·01817	0·08050
20·103	64·486	0·8266	0·04137	0·01787	0·08038
20·200	64·304	0·8266	0·04103	0·01807	0·08028
40·640	36·226	0·8286	0·02420	0·01288	0·05984
60·068	20·607	0·8297	0·01373	0·00856	0·04041
78·417	9·951	0·8306	0·00646	0·00469	0·02206

FIG. 3.



△ Ag–AgCl. ○ Glass. + Ag–AgCl (*Shedlovsky and MacInnes*).

and the points obtained with the glass electrode do not deviate from this line by more than 0·03 mv. The results of Shedlovsky and MacInnes (*loc. cit.*) at the higher dilutions (the right-hand side of the figure) agree less well. This, we suspect, was due to a failure to deoxygenate their solutions since they make no mention of this precaution.

Our results show that two glass electrodes can be used for concentration-cell measurements of high precision. We conclude from this and the preceding paper that in dilute aqueous solutions of a strong acid the glass electrode is capable of yielding results as precise as those which can be obtained with the hydrogen, calomel, or silver–silver chloride electrodes.

The value for B agrees with the value 0·214 mole^{-1} kg. obtained in Part I. That it is slightly lower (corresponding to $\frac{1}{2}$% in γ at 0·1m) than the value 0·234 mole^{-1} kg. calculated from the results of Hills and Ives by Guggenheim and Prue (*Trans. Faraday Soc.*, 1954, **50**, 231) may be significant, since an analysis of the freezing-point data for hydrochloric acid (Guggenheim and Prue, " Physicochemical Calculations," North-Holland Publishing Co., Amsterdam, 1955, p. 223) gives a value for B of 0·216 mole^{-1} kg., again lower than that obtained from cell measurements with the hydrogen electrode at 0°.

We are grateful to Professor E. A. Guggenheim, F.R.S., and to Dr. M. L. McGlashan for helpful discussions of this and the preceding paper.

READING UNIVERSITY. [*Received, May 9th*, 1955.]

Studies in Polymorphism. Part VII. The Linear Rate of Polymorphic Transformation of Cubic to Monoclinic Carbon Tetrabromide.*

By N. H. Hartshorne and P. McL. Swift.

[Reprint Order No. 6075.]

Measurements of the linear rate of transformation of cubic to monoclinic carbon tetrabromide have been made in thin polycrystalline films at temperatures just below the transition point. Previous annealing of the films appears to increase the tendency for the rate to decline at constant temperature. Unannealed films mostly show a constant rate. The rate is much greater than that of the β- to α-transformation of sulphur at the same supersaturation.

The change in the rate with temperature does not follow either the linear law (rate proportional to the supersaturation) or Dunning's equation based on the theory of two-dimensional nucleation. On the basis of the best available value of the transition temperature, the rate very near to this temperature is proportional to the square of the calculated supersaturation, or very nearly so, and on the assumption, by analogy with the sulphur transformation, that the activation energy is of the same order as the sublimation energy, the absolute value of the rate in this region is not inconsistent with the requirements of the dislocation theory of crystal growth at low supersaturations.

Some new optical crystallographic data for monoclinic carbon tetrabromide have been obtained.

It has long been known that carbon tetrabromide undergoes an enantiotropic transformation between a lower-temperature monoclinic phase and a higher-temperature cubic phase (Lehmann, "Molekularphysik," Vol. I, 1888, p. 178). Values given for the transition point (referred to subsequently as T_0) are 46·1° (Schwarz, Preisschrift, Göttingen, 1892, p. 47), 46·2° (Bridgman, *Proc. Amer. Acad. Arts Sci.*, 1915, **51**, 55), 46·9° (Frederick and Hildebrand, *J. Amer. Chem. Soc.*, 1939, **61**, 1555), and 46·91° (Rothmund, *Z. phys. Chem.*, 1897, **24**, 705), of which the last two seem to be the preferred ones (International Critical Tables give 46·9° ± <1°) and are consistent with our own determinations (see below). The m. p. reported by Wahl (*Phil. Trans.*, 1913, **212**, *A*, 117) and by Frederick and Hildebrand (*loc. cit.*) is 92°. Our observations indicate a somewhat higher value than this but we did not determine it accurately.

The main object of this investigation was to determine the linear rate of transformation of the cubic form into the monoclinic form in thin polycrystalline films as a continuation of similar studies described in earlier parts of this series. It was thought possible that, since the parent phase is isotropic, the rate of advance of the interface might show less variance than in the other cases studied (*e.g.*, sulphur, Part VI, *J.*, 1951, 1097). This hope has not been fulfilled, for the variance in the rate has proved to be considerable. Also, the isotropism of the parent phase has prevented observation of its grain size and crystal orientation by optical means, and this has imposed some limitations on the study of the transformation. Further, the rate increases so rapidly as the temperature is lowered from T_0, that it has only been found possible to make determinations corresponding to interface temperatures which are known or can be estimated, over a range of less than 2°. Many attempts were made to "rush" the cubic phase through the temperature range of high velocities to the expected low-velocity region at low temperatures by intense chilling, *e.g.*, by plunging the films into alcohol–solid carbon dioxide, but they were defeated by the very high tendency of the cubic phase to nucleate spontaneously. We have thus been unable to obtain any direct evidence regarding the activation energy of the transformation.

The conclusion reached in the cases of sulphur (*loc. cit.*) and *o*-nitroaniline (Part III, *J.*, 1935, 1860) was that the activation energy involved in the passage of a molecule from

* Part VI, *J.*, 1951, 1097.

the unstable crystal to the transitional layer was of the same order as the heat of sublimation. Later work on sulphur at low temperatures (Hartshorne and Thackray, unpublished work) has confirmed this, and the same conclusion has been reached by Hodkin and Taylor (*J.*, 1955, 489) in a recent study of the II ⟶ I transformation of azoxybenzene. If this is generally the case for transformations in molecular solids, then a high rate with carbon tetrabromide is to be expected, since the internal heat of sublimation of the cubic form at the mean temperature of our experiments can be calculated to be only 11,535 cal./mole, as compared with 22,500 cal./mole for sulphur (*loc. cit.*) and *ca.* 19,000 cal./mole for *o*-nitroaniline (Part III, *loc. cit.*). Comparison of the rates for carbon tetrabromide and sulphur at the same supersaturation (made possible by new data obtained by Hartshorne and Thackray, see above) show, however, that the difference between them is not nearly so great as would be expected if this were the only factor involved, and the matter is discussed later in this paper. Thus at a supersaturation of 0·0042 which exists at 319·4 °K for carbon tetrabromide and 367·2 °K for sulphur, the ratio $\{d_1 \exp(-11{,}535/R \times 319{\cdot}4)\}/\{d_2 \exp(-22{,}500/R \times 367{\cdot}2)\} \approx 10^5$, whilst the ratio of the observed rates ≈ 60 (d_1 and d_2 are the mean lattice spacings).

The above value for the heat of sublimation of the cubic form is derived from the vapour pressures of the liquid determined by Bolas and Groves (*J.*, 1871, **24**, 780) and the heat of fusion determined by Frederick and Hildebrand (*loc. cit.*). The latter authors also found the heat of transition to be 1420 cal./mole, from which the internal heat of sublimation of the monoclinic form is 12,955 cal./mole. Other values reported for the heat of transition are 1590 cal./mole (Marshall, Hart, and Staveley, *Nature*, 1951, **168**, 519) and 1670 cal./mole (Bridgman, *loc. cit.*). The use of either of these, and the correspondingly increased value of the heat of sublimation of the monoclinic form, makes no difference to the order of the results of our later calculations, and for consistency we shall use Frederick and Hildebrand's value.

Despite the narrow temperature range within which study of the rate was possible, the results are of interest as being the first to be obtained in this series so near to a transition point. From the temperature dependence of the rate in this region, some conclusions, admittedly mainly negative, regarding the mechanism of the transformation have been drawn. Some interesting facts about the way in which the monoclinic crystals grow in the cubic phase have been collected. An attempt to determine T_0 as the temperature at which the interface between the two phases is stationary has shown that, within a narrow temperature range, movements of the interface in *both* directions at one and the same temperature occur. Finally, some new optical crystallographic data for the monoclinic form have been obtained.

Experimental

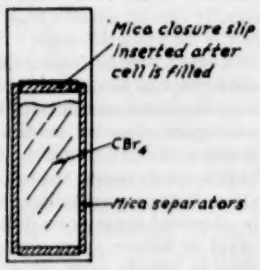
Purification of Material.—The carbon tetrabromide was purified by recrystallisation from alcohol followed by two, or in some cases three, sublimations at low pressure. The sublimation apparatus consisted of a horizontal tube 18 × 1¼ in., closed at one end and connected at the other to a water-pump through a guard tube containing calcium chloride, manometer, and trap cooled by alcohol–solid carbon dioxide. The closed end of the sublimation tube containing the carbon tetrabromide to be purified was heated by an electric coil to 70°. The other end was cooled by allowing cold water to drip on to a cloth wrapped around it, and contained a loosely fitting glass sleeve about 5 in. long to collect the sublimate and facilitate its subsequent removal. The product of this process was colourless and showed no sign of decomposition when heated to prepare the films for the rate measurements, or subsequently.

Preparation of Slides and Films.—Films confined in glass–mica–glass cells as used for the work with sulphur were first tried but did not give reproducible results, probably because the cells were too thick to allow the film to come to thermal equilibrium with the thermostat sufficiently quickly, so that a large amount of rapid lower-temperature growth occurred before this was achieved. Eventually the type of cell shown in Fig. 1 was adopted. This was built up of a 3 × 1 in. slide and a 2 × ¾ in. cover-slip with mica separators, the whole assembly being sealed together with phenol–formaldehyde cement as used in the cells for sulphur. The separators and closure slip (see above) were all cut from the same sheet of mica (0·05 mm.

thick, and subsequent measurements on a number of the filled cells gave values for the film thicknesses ranging from 0·07 to 0·9 mm.

To fill the cells they were placed on an inclined hot plate kept at 100°, so that the bottom of the cell as shown in Fig. 1 was the lower end. The substance was melted in at the open end little by little, the amount being adjusted so that the cell was nearly full. The mica closure slip was then inserted. This slip prevented excessive loss of the substance by evaporation in subsequent operations. The film was allowed to solidify and when required for the rate measurements was converted into the cubic form under controlled conditions as described below.

FIG. 1.



In what follows the prepared cells with their carbon tetrabromide films will be referred to simply as " slides."

Conversion of Films into Cubic Form before Rate Measurements.—For this a modified form of the apparatus described in Part I (*J.*, 1930, 727) for determining the m. p.s of the different polymorphs of *o*-nitroaniline was used. The object of using the apparatus in the present work was to find out for each slide the temperature at which the cubic phase first crystallised and to control its rate of crystallisation as far as possible, in case these conditions should have any influence on the rate of transformation into the monoclinic form. The temperature of the outer bath was first set to 94° ± 0·5°, and the slide was inserted in the inner tube. After melting was complete (usually in 5—15 min.), the temperature was lowered at about 0·1° per min. Crystallisation of the cubic phase always began before the bath temperature had fallen to 93° and was usually complete in 5—10 min. Supercooling thus appears to be very small and it may be deduced that all the films were grown within the same narrow range of conditions of time and temperature.

When crystallisation was complete the slide was either transferred direct to the projection apparatus by means of which the rate was measured or, if it was to undergo a preliminary period of annealing, to a stoppered bottle in an air-oven at 50° ± 1°.

Apparatus for Rate Measurements.—This was the same as that used for sulphur at temperatures above 0°, but owing to the different characteristics of the transformation the procedure for making the measurements had to be modified. In the first place it was necessary to bring the slide to the temperature of the thermostat as rapidly as possible, otherwise it was likely that a considerable area of the film would have been transformed before equilibrium was achieved. The lower part of the inner glass cell of the apparatus was therefore filled to a depth of about 2 in. with clean dry mercury, and on insertion of the slide holder and slide in the cell they were immediately lowered so that the film was immersed in the mercury, and were left there for 1 min. before being raised to the position for projection of the film. This quickly brought the slide to thermostat temperature.

At 45·7°, at which the majority of the measurements were made, the advance of the interface was too rapid to be recorded by tracing on the screen. Since the transformation started by spontaneous nucleation at one or more randomly situated points, and not as in the case of sulphur as the result of deliberate inoculation along a straight start line, it could not be followed by projection on to a grid. Nucleation usually occurred almost as soon as the slide had been placed in the thermostat, or within 20 min. of this, though in one case two hours elapsed before nucleation. The position of the interface was recorded photographically at 5-min. intervals by means of the same camera as was used in the work on sulphur at 0° (*loc. cit.*, p. 1110) except that, in order to take in the whole width of the carbon tetrabromide film on the plate, the opening at the back of the camera had to be widened, and only four records instead of eight could be obtained on one quarter-plate. Since the position of the interface was not sufficiently defined in ordinary light, two polaroid screens were fixed in the path of the light, one in front of, and one behind the thermostat, and were adjusted to be 15—30° from the crossed position. This setting was found to give the best compromise between definition and illumination. Crossed polaroids made the interface invisible at places where the monoclinic crystals were in extinction. Plate I shows an example of the records obtained. These records were subsequently projected on to a screen as in the sulphur work, but the successive positions of the interface were traced, different colours being used to distinguish the different positions. The measurements made on these tracings were the distances advanced by the growing points of the dendritic crystals (see below).

At temperatures nearer to the transition point the transformation was very much slower and

it was then possible to make direct tracings of the positions of the interface on the screen. Spontaneous nucleation did not occur, so that after the slide had acquired the thermostat temperature it was momentarily raised to the top of the cell and the top of the film inoculated by pressing a piece of cold metal against the cover slip. The slide was then at once returned to its proper position. At these temperatures growth was not dendritic and a sufficiently good estimate of the rate could be made by taking measurements on the tracing along a number of equally spaced parallel lines running from top to bottom of the slide, *i.e.*, in the general direction of the interface advance.

Cinephotomicrographic Records of the Transformation.—A number of 16-mm. cinephotomicrographic records of the transformation were taken between crossed Nicols at different magnifications and in both black-and-white and colour. These have proved most valuable for subsequent detailed studies of particular features of the transformation, notably the characteristics of the interesting phenomenon of secondary growth, which is described below. We have come to regard the taking of such films as almost essential in the investigation of transformations between crystalline phases. A particular event, or sequence of events which might never be observed again or be difficult to repeat, is captured once for all and can be studied again and again at leisure. Approximate measurements of the rate can also be made by means of the films in certain cases where the camera speed is known. The projector is focused on a small gridded screen and turned over by hand, the position of the interface being noted, say, every 20 frames. In this way some comparisons between the rates of primary and secondary growth (see later) were made. Under these conditions of use of the projector, the film is protected by a heat filter and so does not suffer.

Results and Discussion

Crystallography of Carbon Tetrabromide and Determination of the Optical Crystallographic Properties of the Monoclinic Form.—The crystal structures of both forms were studied by Finbak and Hassel (*Z. phys. Chem.*, 1937, *B*, **36**, 301). They found 32 and 4 molecules respectively in the unit cells of the monoclinic and the cubic form. The monoclinic cell is pseudo-cubic and may be regarded as derived from 8 of the cubic cells by a very slight distortion. This means that the centres of gravity of the molecules are in nearly the same positions in both forms, and they suggested that the molecules rotate in the cubic form, since it gives very weak *X*-ray reflections. Marshall, Hart, and Staveley (*loc. cit.*) conclude, however, from consideration of their own heat-capacity data for the compound, that the molecules undergo torsional oscillations only in both forms.

The following morphological and optical data for the monoclinic form were obtained by Zirngiebl and are given in Groth's "Chemische Kristallographie," Vol. I, p. 230: $a : b : c = 1{\cdot}7414 : 1 : 1{\cdot}9617$ (which agree reasonably well with the *X*-ray cell dimensions) and $\beta = 125° 3'$. Crystals from acetone are tabular on $c\{001\}$, and have also $r\{10\bar{1}\}$ and $m\{110\}$. Crystals from alcohol are much elongated along b but are still tabular on $c\{001\}$. Cleavages are $c\{001\}$ (perfect) and $b\{010\}$ (pronounced). The optic axial plane is parallel to 010 and an inclined optic axial interference figure is presented by 001.

This information was inadequate to enable us to identify the orientations of the monoclinic crystals in our films under the microscope and we therefore decided to make as complete an optical examination of the compound as possible. Three difficulties at once arose: (1) carbon tetrabromide is readily soluble in the usual immersion media used for determining refractive indices; (2) the usual alternative media for such cases, namely, aqueous-glycerol solutions of potassium mercuric iodide, have a maximum index of about 1·71 and this is lower than both γ and β for the compound; (3) well-formed crystals persistently present the 001 section when mounted in the ordinary way between a slide and cover slip, and examination of other sections is therefore difficult. These difficulties were eventually overcome by using solutions of barium mercuric iodide as immersion liquids and by the use of a single-axis rotation apparatus by means of which a single crystal could be rotated about a given axis while immersed in the liquid. The apparatus together with an auxiliary apparatus for mounting the crystal is described elsewhere (*J. Roy. Microscop. Soc.*, in the press).

The barium mercuric iodide solutions ($BaHgI_4$) were prepared by mixing stoicheiometric quantities of mercuric iodide and iodine with an excess of barium oxide. Water was added

with warming and the residue of barium iodate and barium oxide was filtered off through asbestos. The filtrate was then concentrated under reduced pressure and the most concentrated solution thus obtained had a refractive index of about 1·76, which is considerably higher than γ for carbon tetrabromide. Unfortunately, on exposure to the atmosphere such concentrated solutions take up water vapour and the refractive index falls—rather rapidly if the specific surface of the solution is large. For example, on one occasion when the index of a drop of solution was being measured on a Leitz–Jelley refractometer, the index fell from 1·74 to 1·73 in 2 min. However, by adopting the following procedure and working quickly, values of the principal refractive indices were obtained which are probably accurate to within $\pm$0·001. A crystal from alcohol was mounted on the rotation apparatus so that its long axis (= *b* and β, see data above) was the axis of rotation; α and γ were then determined indirectly by Wood and Ayliffe's method (*Phil. Mag.*, 1936, **21**, 324), which depends on the linear relation between $1/n^2$, where n is the refractive index of the liquid in the cell of the rotation apparatus, and $\cos^2\theta$, where θ is the angle (measured from the position in which the α vibration direction is normal to the axis of the microscope) through which the crystal must be rotated to achieve equality between its index for light vibrating normally to the axis of rotation (the " cross " index) and that of the liquid. This method is at its best when the birefrigence of the crystal is high so that the matching position is sharply defined. In the present case the birefringence is less than 0·02 and it was found that when the ordinary Becke line test was used there was considerable uncertainty about the exact position at which the cross index equalled that of the liquid. However, reasonably reproducible readings were obtained by illuminating the crystal with a narrow pencil of oblique rays produced by two off-centre stops 1/16 in. in diameter, one in the back focal plane of the objective and the other in the conjugate focal plane of the condenser. This arrangement gave a rapid variation in contrast around the matching position and enabled it to be fixed to the nearest 0·5°, which was about the lower limit to which the two-inch drum of the rotation apparatus could be read.

The method of conducting the experiment was to start with a solution in the cell of the apparatus having an index greater than γ for the crystal. The index of the liquid gradually fell by absorption of water vapour from the atmosphere, and as soon it was below γ, readings of θ were begun. Immediately after each reading was taken a drop of the liquid was transferred to the Leitz–Jelley refractometer, and the index measured as rapidly as possible. Throughout the measurements, the composition of the liquid in the cell was kept uniform by frequently partly withdrawing it into a capillary tube and then expelling it back into the cell. Two crystals were studied in this way, and the plot of $\cos^2\theta$ against $1/n^2$ is shown in Fig. 2, which also gives the two best straight lines obtained by the method of least squares, one taking the values of $\cos^2\theta$ as exact and the other the values of $1/n^2$. Both give the same values of α and γ to the third decimal place. The diagram also shows the values of $1/n^2$ corresponding to other near values of n, from which the accuracy of the determination can be judged. The scatter of the points is probably mainly due to the fact that the refractive index of the liquid could not be determined at the same instant as the matching angle was read, rather than to errors in reading this angle.

From a direct measurement of $2V$ (optic axial angle) on the rotation apparatus, the value of β was calculated.* Also the 100 and 10$\bar{1}$ faces were identified from Groth's description (*op. cit.*) and the optic orientation in relation to them determined. The refractive indices were determined in sodium light. The optical data are summarised below and the optic orientation in Fig. 3.

$$\alpha_D\ 1{\cdot}710,\ \beta_D\ 1{\cdot}713,\ \gamma_D\ 1{\cdot}726;\ 2V = 53° \pm 0{\cdot}25°.\ \text{Sign positive.}$$

A useful confirmation that the indices are of the right order is that the mean index $\sqrt[3]{\alpha\beta\gamma} = 1{\cdot}716$, whereas that calculated from the Lorenz–Lorentz equation by use of

* A direct measurement of $2V$ strictly requires that the liquid used in the cell should have $n = \beta$, *i.e.*, that β be known in advance. In our experiments the measured angle varied inappreciably over the short range of refractive indices of the liquids used.

Eisenlohr's refraction equivalents and a density of 3·45 (determined by Marshall, Hart, and Staveley, *loc. cit.*) is 1·718.

Rate Measurements at 45·7°.—The transformation was more extensively studied at this temperature than at any other, and many measurements were made with the object of finding out whether the linear rate was constant and whether it was influenced by previous annealing of the films. The monoclinic phase grows at this temperature in a most interesting way and two distinct processes are involved. The main, or *primary* growth as we shall term it, is dendritic. In our cells it nearly always originated at points on the surfaces of the mica separators. The dendrite branches are large clear crystals which often attain a length of between 10 and 20 mm. and a width of about 1 mm. Following on the heels of this primary growth is a *secondary* growth of small grains which fill the spaces between the primary crystals and also isolated pockets between these and the glass surfaces.

FIG. 2.

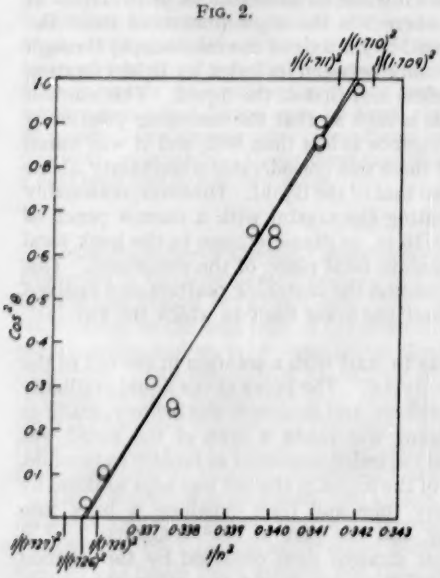
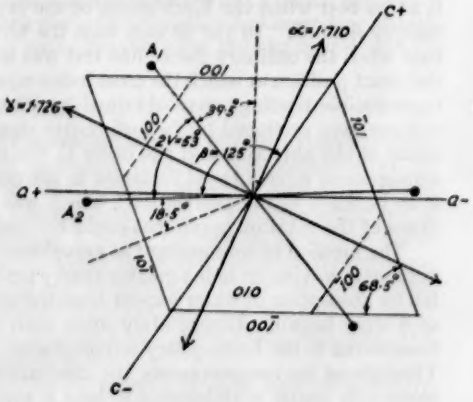


FIG. 3. *Optic orientation of monoclinic carbon tetrabromide on* 010.

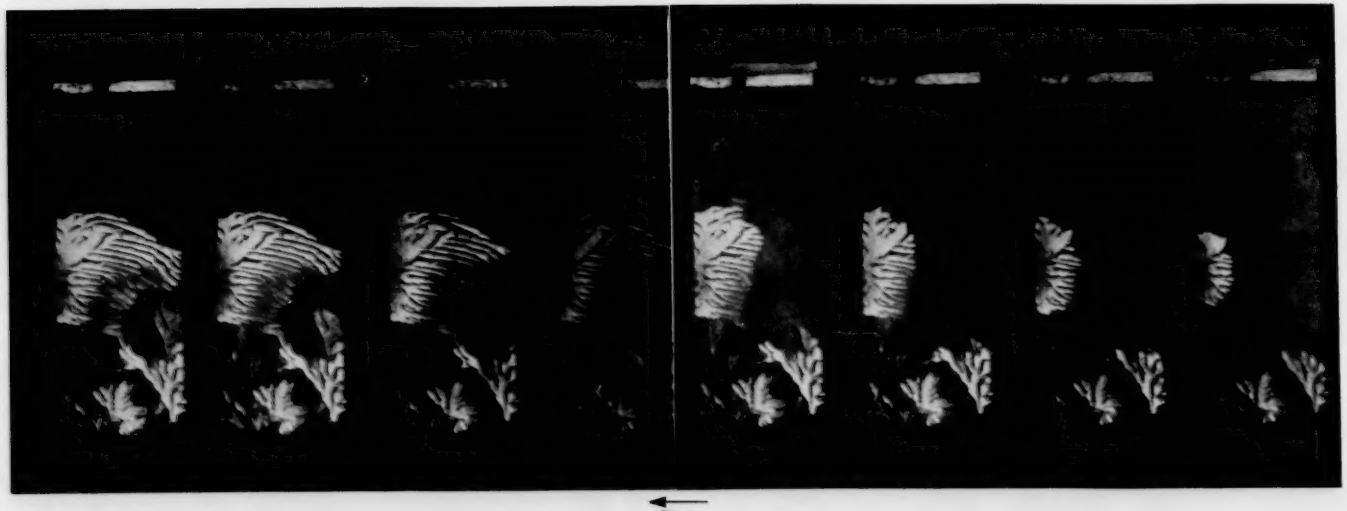


Plates II and III are photomicrographs of a fully transformed film and show clearly the results of the two modes of growth.

A careful microscopic study of the orientations presented by the primary crystals has been made on a large number of the fully transformed films. These orientations have proved to be very varied and appear not to be closely defined by principal lattice planes. Moreover, crystals having a given orientation may have different directions of elongation, and in short, there seems to be no preferred axis of growth. The results of this study are being analysed statistically in order, for example, to ascertain whether the significant differences in mean rate between slides (see below) is traceable to differences in the growth directions of the primary crystals, though there is no obvious sign that any such correlation exists.

The characteristics of the secondary growth have been studied by means of our ciné films and also directly on the hot stage under the microscope. The primary branches as they advance in the direction of elongation also spread laterally, but when the growing tip has passed on, this lateral growth soon comes to a halt, leaving long narrow "inlets" between the branches. Shortly after the lateral growth has ceased, the secondary grains begin to appear. The growth of the grains is spasmodic. Each one grows rather rapidly at first, then slows down and may even stop for a time. It then accelerates or resumes its advance unless in the meantime the surrounding cubic phase has been transformed by

PLATE I.



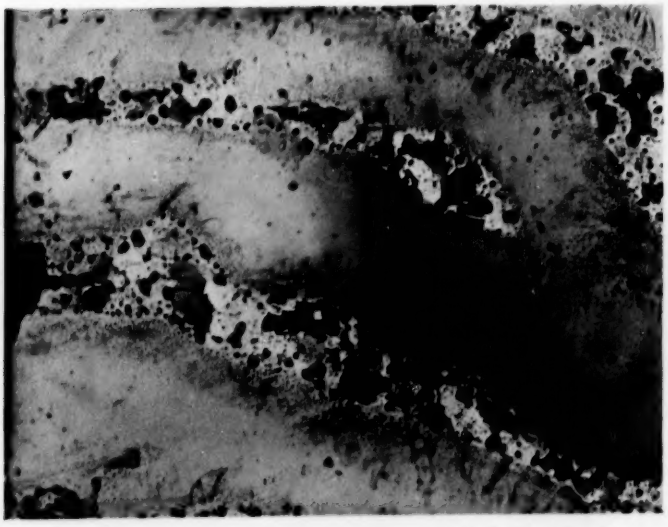
Two quarter-plate records of the same slide at 45·7°. Exposures were made at 5-min. intervals.

[*To face p.* 3710.

PLATE II.

Primary and secondary growth. Between crossed Nicols. (×10.)

PLATE III.



Primary and secondary growth. Between crossed Nicols. (×27—28.)

the growth of neighbouring grains. The grains always seem to originate from the surfaces of the primary crystals but usually to have quite different orientations from them. The filling up of the inlets by this process nearly always occurs some distance behind the growing tips of the primary crystals. The appearance of secondary crystals between the primary crystals and the glass surfaces as seen between crossed Nicols is accompanied in many cases by a fall in the polarisation colour, or even complete compensation, over the area which they cover, thus demonstrating very beautifully that they are differently orientated from the substrate.

The cause of the secondary growth is not obvious. The formation of the inlets in which it occurs is probably a temperature effect. The heat of transformation is fairly high for a polymorphic change, and the rate of transformation as expressed by the rate of advance of the tips of the dendrite branches is of the order of 15 mm./hour, *i.e.*, about three times the maximum rate observed for sulphur (Part VI, *loc. cit.*). Moreover, this high rate occurs at a temperature which is only 1·2° below the transition point, so that the temperature coefficient is very large. Calculations by means of Davidson's equation (Part VI, *loc. cit.*) show that the rise of temperature at the interface under these conditions could amount to about 0·06° for an infinite linear interface, and it is therefore not unlikely that the lateral growth of neighbouring branches would be very much slowed down or even temporarily stopped by the development of heat which could not flow away fast enough. But as the advancing tips of the branches push further ahead these retarded or halted parts left behind must cool again to thermostat temperature, and one would expect that the growth of the original crystal would then simply be resumed. Instead, a crop of quite differently oriented crystals (the secondary grains) appears although, within the limits of microscopic resolution, they appear to originate at the surfaces of the primary crystals. Very careful attempts were made to ascertain whether there was any sign of strain birefringence in the inlets before secondary growth occurred. The isotropism of the cubic phase here offered an advantage. Intense illumination and carefully crossed Nicol prisms were used, and the field was examined after insertion of a first-order red selenite plate, but the results were negative. We are therefore forced to the conclusion that, when lateral growth of the primary branches ceases, some actual discontinuity in the structure arises at the interface and that the secondary growth, though appearing to originate from the halted surface of the primary crystals, actually represents the result of three-dimensional nucleation of the opposite side of the discontinuity. Any suggestion that the secondary grains are another modification of carbon tetrabromide may be dismissed, since films having the structures shown in Plates II and III have been preserved for over four years without apparent change.

Some rough comparisons of the rates of primary and secondary growth were made by slow projection of the ciné films as mentioned on p. 3708. The mean linear rate for the secondary granules was of the same order as the rate of advance of the growing tips of the primary branches, but the initial rate of growth of the granules was considerably greater than this.

The measurements of primary growth made on the tracings were the rates of advance of the growing tips of the primary branches, as already stated. These were the only measurements which could conveniently be made. The results of the studies of orientation and directions of elongation referred to above, indicate, however, that these directions of growth probably covered a wide range of lattice directions. Moreover, since the growing tips had an " open sea " of the cubic form ahead of, and partly around, them, the heat of transformation must have been much more rapidly dissipated from them than from the inlets between the branches. It seems likely, therefore, that their temperature was not appreciably different from that of the thermostat, or at least that the result of applying Davidson's equation represents an upper limit to the temperature rise.

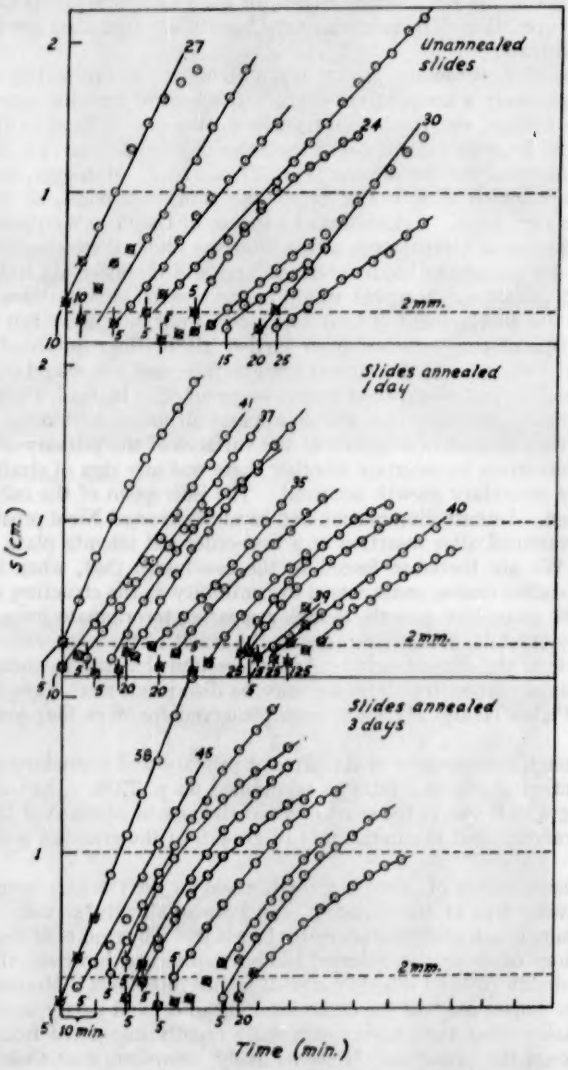
Three series of slides were studied as follows: (1) unannealed slides, *i.e.*, slides transferred direct from the crystallisation apparatus to the projection apparatus, (2) annealed slides, which after being removed from the crystallisation apparatus were transferred to a stoppered bottle in an air oven at 50° ± 1°, and left there for either (*a*) 1 day or (*b*) 3 days before being transferred to the projection apparatus.

Figs. 4, 5, and 6 give the t–s plots for individual slides in the three series, where t is the time (the time of insertion of the slide in the thermostat being taken as zero) and s is the "average distance" advanced. The latter was obtained by progressive addition of the mean advances (Δs) for successive intervals of 5 min. (see p. 3707). The s scale thus set up

FIG. 4.

FIG. 5.

FIG. 6.



is to some extent fictitious since on many slides crystals grew from two or more centres and these started at different times. Thus crystals originating from the later centres would have high t values and low true s values, but their results would be pooled with those of crystals from earlier centres which by this time would have achieved higher s values. (New crystals resulting from branching can be regarded as having the same origin as the

parent stem.) The t–s plots afford, however, a convenient means of showing whether there was any trend in the rate with time.

The number of measurements on which the majority of the individual Δs values were based varied between 1 and 25. Points in Figs. 4—6 based on less than 5 measurements are distinguished by a superposed cross, and little or no weight has been given to these points in drawing the smoothed plots.

The origins of the plots have been distributed along the time axis in order to avoid superposition and confusion. The figure at the foot of each plot gives the t value (to the nearest 5 min.) for the first point. Thus for a slide which nucleated at once on insertion in the thermostat the first point is marked " 5," whilst for one which did not nucleate until 10 min. after insertion it is marked " 15 " and so on.

In the unannealed series (Fig. 4) all the plots are good or reasonably good straight lines (27 and 30 shows a slight decline at high t values) except that for slide 24, which shows a continuous decline of rate with t. In the 1-day series, slides 41, 37, 40, and probably 39 give straight lines and the others show declines, with the exception of 35 which shows a slight rise of rate with t. In the 3-day series, 58 and 45 give straight lines and the remainder show a decline. There is thus an increasing proportion of cases in which the rate declines with time in the direction : unannealed, annealed one day, annealed three days.

This decline could (1) be a real effect, meaning that *individual crystals* show a progressive decline in rate owing, say, to shrinkage resulting from the difference in density between the two forms (as suggested for *o*-nitroaniline, Part III, *J.*, 1935, 1860, and mercuric iodide, Part IV, *J.*, 1938, 1636) or could (2) result from the way in which the results are grouped. Thus even if individual crystals grow at a constant rate but those which start late are slower than the earlier ones, the s–t plot must necessarily show a decline. Measurements of the rate of advance of a number of single crystals made on the tracings (those crystals being selected which could be followed for the longest possible time so that any trend would not be obscured by local variances) and a qualitative examination of the tracings for evidence of the effect of grouping have shown that in fact both this and real declines in the average rate of some crystals do occur. It has not, however, proved possible to disentangle the two effects completely. Thus in a number of slides which nucleated near the upper solid–vapour interface of the film the monoclinic phase spread preferentially along this interface and developed a progressively increasing number of crystals growing inwards which were slower than those in the body of the film. In no such case, however, was it possible to say that the decline was due to this cause alone, because either the single crystals measured on the slide themselves showed a decline or else no acceptable single-crystal measurements covering a large t range could be made.

It should be noted that the range of s values covered by most of the slides, namely, 10—20 mm., far exceeds that in previous studies in this series. In the cases of *o*-nitroaniline and mercuric iodide (Parts III and IV, *locc. cit.*), which showed a marked decline of rate, the maximum s range was of the order of 1 mm. In the sulphur transformation (Parts V and VI, *J.*, 1940, 588; 1951, 1097), in which the rate was constant, it was about 2 mm. It may well be that if it had been possible to confine the measurements on carbon tetrabromide to such narrow s ranges no decline would have been detected, for the rate of decline was much smaller than was found in the earlier studies. For example, in slide 24 (Fig. 4) the average rate fell to half its initial value after an advance of about 10 mm., whilst with mercuric iodide a similar relative decline occurred for an advance of only about 0·5 mm. The initial 2-mm. interval is indicated by horizontal lines on Figs. 4—6, and rough extrapolation of the smoothed plots to $s = 0$ shows how small a change of rate would have occurred over this interval.

A possible explanation of the constant rates shown by almost all the unannealed slides and of the increase in the incidence of cases of decline of rate with annealing is as follows. In the unannealed slides, the fairly rapid descent from the temperature of the crystallisation apparatus to that of the thermostat may have resulted in the formation of a granular cubic film in which the transformation started afresh, as it were, at each grain boundary, so that whatever the tendency of the rate to decline while the interface was traversing a single grain, it was on the average constant. It may then be supposed that the annealing

process applied to the other slides would result in grain growth of the granular film leading to the formation of much larger homogeneous domains, in traversing which the interface would suffer a decline in its rate of advance owing to the shrinkage resulting from the density change accompanying the transformation. (The densities are: cubic 3·21, monoclinic 3·45; Marshall, Hart, and Staveley, *loc. cit.*) If the sizes of these domains were comparable with the total advance measured, this decline would be reflected in the average rate of advance.

The rise in rate shown by the plot of slide 35 (Fig. 5) is difficult to account for. Examination of the tracing showed that it was not due to any grouping effect but to a rise in the rate of advance of some of the single crystals. Other crystals on the slide showed a constant rate.

It seemed to be very difficult to make any quantitative use of the results obtained on slides which showed a non-constant rate, and we therefore decided to take the constant or near-constant results obtained with the unannealed slides (except No. 24) as the " normal " case, and to make all subsequent measurements at other temperatures on unannealed slides. The mean rates of these eight slides ranged from 9·4 to 22·4 mm./hr. Analysis of variance of the single Δs measurements showed that the ratio of the variance between slides to that within slides was 96·6, which is very highly significant, showing that the sets of measurements representing the individual slides cannot be regarded as random samples from the same population. We must therefore treat the slide means as single measurements in assessing the probable limits within which the true mean lies. The slide means being taken as of equal weight, which is justified since each is based on a large number of Δs measurements (minimum 61, maximum 185), this leads to a grand mean of 14·8 mm./hr. with 95% fiducial limits of $\pm$4·2. The coefficient of variation of the slide means was 0·35.

The limits of the thermostat temperature during these measurements were about $\pm$0·025°. Allowing for the possibility that the interface temperature might be up to 0·06° higher than that of the thermostat (see above), this makes the limits of uncertainty 45·675—45·785°.

Determination of T_0.—Since the exact value of T_0 seemed to be in need of confirmation, and would be required for the accurate calculation of the supersaturation, we attempted to determine it with our apparatus by seeking the temperature at which the interface was stationary. This involved keeping the interface under observation at different temperatures for long periods, often of some days. The position of the interface was recorded either by tracing on the screen (magnification factor 21·5) or in later experiments by darkening the whole room and exposing a photographic plate carried in a dark slide affixed to the screen. In the latter method a transparent grid of 0·5 mm. squares was attached to the slide and appeared in the photographs as a reference net against which very small changes in the position of the interface were immediately obvious.

In preliminary experiments at bath temperatures ranging from 46·78—46·83° to 46·93—46·98° and lasting from 4 to 17 hours, it was found that, although the interface remained stationary over most of its length, it advanced (*i.e.*, cubic transformed to monoclinic) in some parts and retreated in others. Below this range only advances were observed, or advances with some parts stationary, while above it the interface was observed to retreat, or the monoclinic crystals showed interior regions of general conversion into the cubic form. [Spontaneous transformation to this form occurs without noticeable superheating, and as seen between crossed Nicols the process looks more as though the monoclinic crystals were melting than undergoing a solid–solid transformation. Wahl (*loc. cit.*) also reported this behaviour.] The temperature control was then improved to $\pm$0·01° or better, but in an experiment at 46·88—46·89° lasting 3 days the same phenomenon of simultaneous advances and retreats of the interface was observed.

The specimen of carbon tetrabromide so far used had been sublimed twice. It was thought possible that the effect might be due to traces of impurity unequally distributed throughout the film, though phase-rule considerations show that a second component could only affect the value of T_0 if it formed solid solutions with the carbon tetrabromide. Further experiments were therefore done with a specimen which had been sublimed three times but the same effect was observed at 46·92—46·94° (4 days) and 46·96—46·98° (2 days),

though the movements (which were of the order of 0·01—0·1 mm.) were not so marked as with the earlier specimen, and in two other experiments at 46·92—46·95° (3 days) and 46·92—46·94° (1 day) no movement either way was detected.

The only other difference between the behaviour of the two specimens was that the one sublimed three times showed advances only at 46·82—46·84° which lies within the range in which the twice-sublimed specimen showed both advances and retreats in the preliminary experiments, but this difference may have been due to the better temperature control in the later work. Observations on the hot stage of the microscope, in which closely adjacent edges of films of the two specimens were watched while the temperature was very slowly raised, failed to detect any difference in the point at which conversion into the cubic form began, and there seems little doubt that the specimens were very similar and of a high degree of purity.

A more likely explanation of the simultaneous advances and retreats is that the movements are caused by small free-energy differences arising from localised strains in the two structures, and they may possibly be a manifestation of the "indeterminacy" in phase transitions postulated by Ubbelohde (see, *e.g.*, *Nature*, 1952, **169**, 832). It is hoped to investigate the phenomenon more closely.

Even if these small movements be disregarded as being a purely local effect, it is evident that the method, at least with the present apparatus, is not capable of giving a precise value for T_0, since the range of temperature over which most of the interface showed no detectable movement was (taking all our experiments) about 0·2°. This is certainly due to the fact that, as will presently appear, the linear rate (v)–temperature (T) curve tends to $dV/dT = 0$ at T_0, so that the rate must be inappreciable over a finite range of temperature near this point. Indeed, if the advance of the stable phase is analogous to growth from a vapour (see below), it may actually be halted over a finite temperature range because the growth mechanism is "frozen." For example, the dislocation theory of crystal growth predicts that at extremely low supersaturations growth must cease because the critical nucleus is too large to pass between adjacent dislocations (see Frank, *Phil. Mag.*, *Suppl.*, 1952, **1**, No. 1, 91).

The values for T_0 given by Frederick and Hildebrand and by Rothmund (*locc. cit.*) are consistent with the above observations, and for the present we shall take the rounded value of 46·90°.

Linear Rate between 45·7° and T_0.—The Table summarises the results of all the measurements made on unannealed slides. At temperatures other than 45·7° the number of

Linear rate measured on unannealed slides.

Thermostat temp.	Mean rate (mm./hr.)	No. of slides studied	95% Limits	Thermostat temp.	Mean rate (mm./hr.)	No. of slides studied	95% Limits
45·7° ± 0·025°	14·8	8	10·6—19·0	46·53° ± 0·01°	0·12	1	—
46·23 ± 0·01	0·735	1	—	46·64 ± 0·01	0·094	3	>0—0·283
46·30 ± 0·01	0·71	1	—	46·74 ± 0·01	0·029	3	>0—0·067
46·33 ± 0·01	0·67	1	—	46·83 ± 0·01	0·009	1	—
46·44 ± 0·01	0·37	3	0·29—0·46				

measurements made on each slide was not large (14—21 in most cases) and, as already stated (p. 3708), the method of measurement was different since the growth was not dendritic, but they were sufficient to give a good estimate of the slide mean rate. In the light of the results at 45·7° the slide means have been treated as single measurements and for temperatures at which more than one slide was studied the 95% limits are given. The assumption was made that the rate was constant and this was justified by the results obtained on a number of the slides on which the advance for more than one time interval was measured. In these, although the results for successive intervals showed considerable variance as was to be expected, there was, taking the slides as a whole, no trend of rate in either direction.

The results are plotted in Fig. 7. The frame drawn round the 45·7° point is defined by the 95% limits and the uncertainty regarding the interface temperature mentioned above.

The 95% limits at other temperatures, where these limits were calculated, are also indicated on the Figure. The uncertainty regarding the temperature co-ordinates of these and the neighbouring points is practically negligible on the scale of the Figure, since the thermostat temperature was controlled to $\pm 0{\cdot}01°$, and the rates were so low that there was no question of a detectable self-heating effect.

The curve approaches T_0 (which we have taken in the figure as 46·90°) asymptotically, and, as shown below, this rules out the possibility that it follows any equation of the general form of those proposed by Akulov (*Compt. rend. Acad. Sci. U.R.S.S.*, **1941**, **32**, 340; **1943**, **39**, 268), Laurent (*Rev. Metall.*, **1945**, **42**, 22), and by one of us (N. H. H.) [*Discuss. Faraday Soc.*, **1949**, **5**, 149, equation (3)]. All these equations involve the assumption that

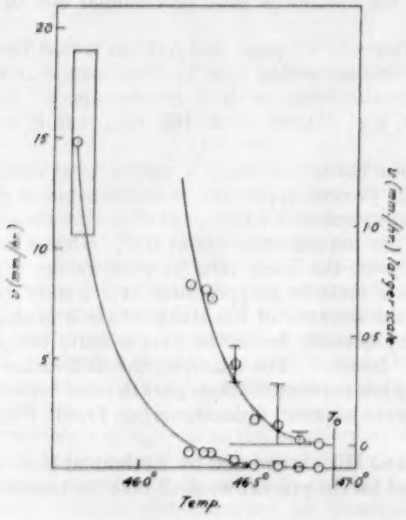


FIG. 7. *Right-hand curve shows results for temperatures above 46° plotted on a larger v scale.*

every molecule which arrives at the surface of the growing phase contributes to its growth, and as shown in the last-mentioned paper, near T_0 they approximate to the form

$$v = \text{const.}\ (-\Delta G/T)\ \exp\ (-E/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

(except that Akulov's equation contains no explicit reciprocal T factor), where v is the linear rate, $-\Delta G$ is the free-energy change attending the transformation, E is the potential barrier which the molecules must surmount in passing from the unstable to the stable structure, and the other symbols have their usual significance. Substituting $q(T_0 - T)/T_0$ for $-\Delta G$, where q is the heat of transformation, and differentiating, we find that, when $T = T_0$, $\mathrm{d}v/\mathrm{d}T$ is finite. Furthermore, in the very short temperature range just below T_0 which we are considering, by far the most important variable is $(T_0 - T)$, so that the plot of v against T should be very nearly a straight line. The experimental curve obviously does not fulfil these conditions.

In the Faraday Society Discussion (*loc. cit.*), it was shown that deviations in the rate of transformation of β- to α-sulphur from the requirements of Hartshorne's equation (3) (mentioned above) could be accounted for by the introduction of a semiempirical factor ϕ, which represented a supposed increase in the rate of escape of molecules from the α-form* owing to its fine state of division. This correction applied mainly to the region below the temperature of maximum velocity, in which the fine serrations on the front of the advancing rhombic phase were obvious, and it would be quite unrealistic to treat the present case

* In the derivation of the equation given in the Discussion section the symbols α and β denoted the unstable and stable forms respectively. In order to conform with the accepted designations of the forms of sulphur, they are used here in the reverse sense.

similarly, for just as has been observed in the case of sulphur near to the transition point, the growing crystals are large and exhibit few surface irregularities when viewed under the microscope.

If we assume, by analogy with the results obtained with sulphur (Part VI, *loc. cit.*) and the other molecular solids mentioned earlier, that the activation energy is the same as the heat of sublimation, we must suppose that the transitional layer at the interface is populated by molecules which are energetically equivalent to molecules in the vapour state. We may, in fact, treat the transformation process as being essentially one of growth of the stable phase from a vapour at a supersaturation determined by the vapour pressure of the unstable form. This picture does not require that the two solids be separated by a thick layer having the properties of a gas in bulk, so that the molecules suffer collisions in transit, though this state of affairs could arise at a late stage in the reaction owing to shrinkage resulting from the higher density of the stable form. If the solids are only one or a few molecular diameters apart, then molecules which leave the unstable form forthwith strike the surface of the stable form (as originally pictured in Part III, *loc. cit.*), and the rate at which they do this will be equal to the rate at which molecules would return to the unstable form if it were in contact with its saturated vapour in bulk. This rate is proportional to the vapour pressure multiplied by the condensation coefficient. If this coefficient is unity, and it is nearly so for many solids, it follows that (returning to the case under consideration) the rate of impact on the surface of the stable form will be the same as if it were in contact with free vapour at the vapour pressure of the unstable form.

We shall therefore now consider the results in terms of the modern dislocation theory of crystal growth from the vapour (Burton, Cabrera, and Frank, *Phil. Trans.*, 1950—51, **243**, *A*, 229). This theory predicts that when the mean migration distance of an adsorbed molecule on the surface of the growing crystal is greater than half the distance between successive turns of the spiral growth step, the rate of growth will be proportional to the first power of the supersaturation. This is the so-called "linear law" which may be stated as

$$v = Cx \exp(-L_I/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

where C is a constant which in the simplest case is the product of the step height (d) and the vibration frequency (ν) of the surface adsorbed molecules in the crystal, L_I is the latent heat of sublimation of the crystals, and x is the supersaturation. Now

$$x = p_{II}/p_I - 1 = \exp(-\Delta G/\boldsymbol{R}T) - 1 = \exp[q(1/T - 1/T_0)/\boldsymbol{R}] - 1$$

where p_{II} is the pressure of the supersaturated vapour, and p_I the vapour pressure of the growing crystal, and the other symbols are as defined above. Applied to the present case, p_{II} is the vapour pressure of the unstable form, and substituting in (ii) we obtain :

$$\begin{aligned} v &= C \exp(-L_I/\boldsymbol{R}T)\{\exp[q(1/T - 1/T_0)/\boldsymbol{R}] - 1\} \\ &= C \exp(-L_{II}/\boldsymbol{R}T) \cdot \exp(-q/\boldsymbol{R}T) \cdot \{[\exp(q/\boldsymbol{R}T)/\exp(q/\boldsymbol{R}T_0)] - 1\} \\ &= C \exp(-L_{II}/\boldsymbol{R}T) \cdot \{1 - \exp[q(1/T_0 - 1/T)/\boldsymbol{R}]\}/\exp(q/\boldsymbol{R}T_0) \quad . \quad . \quad \text{(iii)} \end{aligned}$$

where L_{II} is the latent heat of sublimation of the unstable form. Now C has the same significance as the factor A_β in the derivation of Hartshorne's equation (3) (*loc. cit.*), and apart from the existence of an additional pre-exponential factor of $\frac{1}{2}$ in that equation,* it and the above equation (iii) are identical in form. Hartshorne's equation is, in fact, a general form of the linear law applied to a polymorphic transformation, and, as has been shown above, it cannot apply to the present results.

At very small supersaturations the dislocation theory shows that the turns of the spiral growth step will become greater than the mean migration distance of adsorbed molecules,

* For a vapour transitional layer this factor is only applicable if the layer is thick enough to behave as a gas in bulk (assuming that the condensation coefficients for the two forms are equal) (R. S. Bradley; unpublished work).

and predicts that the rate of growth will then be proportional to the *square* of the supersaturation (the so-called " parabolic law "). The equation may now be written as

$$v = (Cx^2/x_1) \exp(-L_I/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iv)}$$

where C is the same as in (ii), and x_1 is a quantity called the critical supersaturation which at constant temperature has the significance that at supersaturations much below it the parabolic law is obeyed, whilst at supersaturations much above it growth follows the linear law (Burton *et al.*, *loc. cit.*). The other symbols have the same significance as before. x_1 is not temperature independent since it contains as factors $\exp[-(W'_s - U_s)/2\boldsymbol{k}T]$ and $1/T$, where W'_s is the evaporation energy of a surface-adsorbed molecule, and U_s is the activation energy required for such a molecule to migrate from one lattice site to an adjoining one, $\boldsymbol{k}$ being Boltzmann's constant. It also contains the edge free energy of the growth step as another factor. For a close-packed crystal, such as calculations based on Finback and Hassel's X-ray results (*loc. cit.*) show carbon tetrabromide to be, $(W'_s - U_s)/2$ is estimated by Burton *et al.* to be somewhat less than one-third to one-fourth of the total evaporation energy (per molecule), and so when the latter is not very large, as for carbon tetrabromide, the exponential factor will not change much over a small range of temperature. Its change is also partly compensated by that of $1/T$ though the effect of this is very small. Within the short range of temperature near T_0 which is now under consideration, calculations show that we can certainly ignore the variation in x_1 in comparison with that of x, so that (iv) reduces to

$$v = C'x^2 \exp(-L_I/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(v)}$$

where C' is a constant. Furthermore since x is very small, we have that

$$x = \frac{p_{II}}{p_I} - 1 \approx \ln \frac{p_{II}}{p_I} = -\frac{\Delta G}{\boldsymbol{R}T} = \frac{q}{\boldsymbol{R}T_0}\left(\frac{T_0 - T}{T}\right)$$

and substituting in (v) we obtain

$$v = C'\left(\frac{q}{\boldsymbol{R}T_0}\right)^2 \left(\frac{(T_0 - T)}{T}\right)^2 \exp(-L_I/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad \text{(vi)}$$

or

$$\ln v + \frac{L_I}{\boldsymbol{R}T} = 2 \ln\left(\frac{T_0 - T}{T}\right) + \ln C'' \quad . \quad . \quad . \quad . \quad . \quad \text{(via)}$$

where C'' is another constant which includes the factor $(q/\boldsymbol{R}T_0)^2$. By differentiating (vi) we find that when $T = T_0$, $dv/dT = 0$, and the same result is obtained if the full equation for the parabolic law is so treated, so that the result is not simply a consequence of the approximations which have been made. This condition is satisfied by the experimental curve (Fig. 7).

From (via) it follows that the plot of $\ln v + L_I/\boldsymbol{R}T$ against $\ln[(T_0 - T)/T]$ should be a straight line with a slope of 2. This plot is shown in Fig. 8 (Curve A), from which it is seen that the points conform to this requirement reasonably closely, with the exception of the point for 45·7° (P), though it is possible, as shown, to pass a fairly well-fitting curve through all the points. The result near T_0 is naturally very sensitive to the value taken for T_0, and a change in this of ±0·05° gives quite a different slope to the lower end of the curve. An increase of 0·01°, however, which represents the difference between the rounded value of 46·90° here assumed, and Rothmund's value of 46·91° (*loc. cit.*), makes no essential difference to the slope.

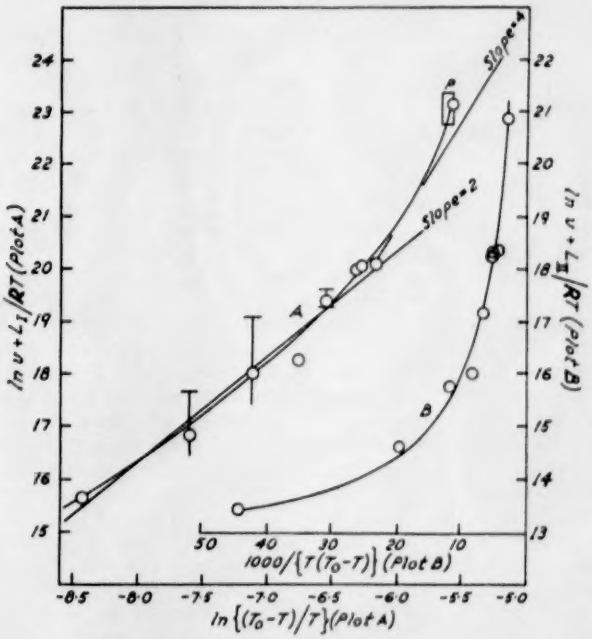
The two-dimensional nucleation mechanism proposed by Dunning (*Discuss. Faraday Soc.*, 1949, **5**, 194) does not account for the experimental curve, and it is hardly to be expected that it would apply at such very small supersaturations. Dunning's equation may be written as

$$\ln v = (\text{const.})_1 - \frac{L_{II}}{\boldsymbol{R}T} - \frac{(\text{const.})_2}{T(T_0 - T)} \quad . \quad . \quad . \quad . \quad . \quad \text{(vii)}$$

Differentiation shows that when $T = T_0$, $dv/dT = 0$ as for equation (vi), but the equation also requires that the plot of $\ln v + L_{II}/\boldsymbol{R}T$ against $1/\{T(T_0 - T)\}$ is a straight line. This plot is shown in Fig. 8 (*B*) and obviously does not fulfil this requirement irrespective of whether the point for 45·7° (the uppermost) is considered or not. The strong curvature of the plot is not appreciably affected if values ranging from 46·85° to 46·95° are assumed for T_0.

In these tests of equations (vi) and (vii), the values used for L_I and L_{II} are the internal latent heats of sublimation derived as explained on p. 3706, namely, 11,535 and 12,955 cal./mole, respectively. As far as the results of these tests are concerned, however, it makes practically no difference what values are taken for these quantities, provided that they are not considerably greater than those just stated. In the test of equation (vi) only 1% of the total change in $\ln v + L_I/\boldsymbol{R}T$ is due to the change in the second term, and in

FIG. 8.



the test of Dunning's equation the change in $L_{II}/\boldsymbol{R}T$ represents less than 1% of the total change in $\ln v + L_{II}/\boldsymbol{R}T$. The conclusions reached would therefore be equally valid for any mechanisms described by equations similar to these, but involving growth from a transitional layer which molecules could enter without acquiring the full sublimation energy. We will, however, continue to pursue the consequences of the assumption that the growth of the stable phase is a process analogous to that of growth from a vapour phase. On this basis the only mechanism of those mentioned above which might possibly account for the results at the lower supersaturations is that expressed in the parabolic law in dislocation theory. The difficulty here is that with increasing supersaturation the rate tends to a dependence on a higher power of the supersaturation than 2 (the upper part of the curve *A*, Fig. 8, has a mean slope of 4—5), whereas dislocation theory requires that the change should be in the opposite direction, *i.e.*, from the parabolic law to the linear law. The observed effect may be due to the fact already mentioned that in our experiments the growth at 45·7° (point *P*) was dendritic whilst that at the higher temperatures was not, so that the results for the latter may not be really comparable with those at 45·7°. Recent measurements of the rate of transformation of β- into α-sulphur near the transition point

(Hartshorne and Thackray, see above) indicate, however, a very similar dependence of the rate on supersaturation to that now described. Thus between 80° and 90° the mean rate is approximately proportional to the fourth power of the supersaturation, and between 90° and the transition point 95·5° ± 0·1°, a reasonable interpolation gives rates which are approximately proportional to the square of the supersaturation.

Although the change to a higher power in the dependence of the rate on supersaturation with increase in the latter does not conform to dislocation theory, and we can at present offer no satisfactory explanation of this change, the fact that at the the lowest supersaturations the rate appears to be proportional to the square of the supersaturation (as is required by this theory), or nearly so, justifies a closer examination of the application of equation (iv) to the results in this region.

Substituting $d\nu$ [see equation (ii)] for C in equation (iv), we obtain

$$v = (d\nu x^2/x_1) \exp(-L_I/\boldsymbol{R}T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(viii)}$$

Taking for d the average spacing between the molecules in monoclinic carbon tetrabromide, namely, $5{\cdot}4 \times 10^{-8}$ cm., and for ν 10^{12}—10^{13}, say, 5×10^{12} sec.$^{-1}$, then we have at 46·3° (which is just inside the range in which the rate is approximately proportional to x^2), $x = 0{\cdot}0042$ and v works out to $2{\cdot}5/x_1 \times 10^{-1}$ mm./hr. Now Burton *et al.* (*loc. cit.*) estimate that a typical value for x_1 would be 10^{-1}, and calculations that we have made indicate that for carbon tetrabromide it would probably be between 10^{-1} and 10^{-2}. This would place v between *ca.* $2{\cdot}5 \times 10^{-3}$ and $2{\cdot}5 \times 10^{-2}$ mm./hr. The observed value (Fig. 7) is *ca.* 6×10^{-1} mm./hr., which is considerably greater.

The product $\nu \exp(-L_I/\boldsymbol{R}T)$ in equation (viii) represents the rate of arrival of vapour molecules at single lattice sites from the vapour at the *equilibrium* pressure (see Frank, *Phil. Mag. Suppl.*, **1952**, **1**, No. 1, 91, for a treatment of the theory which emphasises the significance of this part of the equation), and if the condensation coefficient is unity, it must also be equal to the average rate of escape of molecules per lattice site from the surface into the vapour. R. S. Bradley has found, however, that in the case of rhombic sulphur, the rate of evaporation in a hard vacuum is *ca.* 10^4 times greater than that corresponding to the above product (*Proc. Roy. Soc.*, 1951, *A*, **205**, 553), but that the rate agrees with that calculated from the Langmuir expression $\alpha p(2\pi M\boldsymbol{R}T)^{\frac{1}{2}}$ (*J. Amer. Chem. Soc.*, 1916, **38**, 2221), where p is the vapour pressure, and M the molecular weight, if α, the condensation coefficient, is taken as 0·7, *i.e.*, near unity. Now an approximate value for the vapour pressure of monoclinic carbon tetrabromide at 46·3° can be obtained by extrapolation from the vapour-pressure data for the liquid (Bolas and Groves, *loc. cit.*) and the heats of fusion and transition (Frederick and Hildebrand, *loc. cit.*); it is 2·95 mm. of Hg. Calculating the rate of arrival of molecules at single lattice sites from this by means of the Langmuir expression (assuming $\alpha = 1$), and using this value in the calculation of v in place of that given by $\nu \exp(-L_I/\boldsymbol{R}T)$, we find that $v = 3{\cdot}3/x_1 \times 10^{-2}$ mm./hr., which is in much better agreement with the experimental value, if the same assumptions regarding x_1 are made as before. Calculation by the same method for the slightly higher temperature of 46·5° ($x = 0{\cdot}0028$) gives $v = 1{\cdot}5/x_1 \times 10^{-2}$ mm./hr. The observed value at this temperature is $\approx 2 \times 10^{-1}$ mm./hr. We are indebted to Dr. R. S. Bradley for having suggested this method of calculation.

The results at the lower supersaturations are thus not inconsistent with the requirements of dislocation theory, but in view of the marked deviation from these requirements shown by the experimental curve at the highest supersaturation studied (0·0084 at 45·7°) it is felt that the agreement shown by the above values should for the present be treated with considerable reserve.

One of us (N. H. H.) thanks the Council of the Chemical Society for a Research Grant. We are greatly indebted to Dr. B. L. Welch for assistance with the statistics of this problem, and to Dr. R. S. Bradley for many helpful suggestions and criticisms made during the course of the work.

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The Nature of the Internal Hydrogen Bond. Part II. Electronic Spectra of 2-Nitrosoanisole and 6-Methoxyiminocyclohexa-2 : 4-dienone (o-Benzoquinone 1-Monoxime Methyl Ether) and their Derivatives.*

By A. Burawoy, M. Cais, J. T. Chamberlain, F. Liversedge, and A. R. Thompson.

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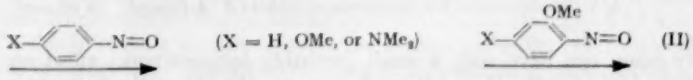
The spectra of nitrosobenzene, 2-nitrosoanisole and its 5-methoxy- and 5-dimethylamino-derivatives, and 6-methoxyiminocyclohexa-2 : 4-dienone and its 3-methoxy- and 3-dimethylamino-derivatives in a series of solvents are analysed. A qualitative interpretation of the electronic transition responsible for *B*-bands is given.

Investigation of the electronic spectra of organic molecules has established that there are two principal types of absorption bands above 2000 Å (*R*- and *K*-bands) which are distinguished by different intensities ($\varepsilon < 2000$ and > 5000, respectively) and optical rules (Burawoy, *Ber.*, **1930**, **63**, 3155; **1931**, **64**, 464, 1635; **1932**, **65**, 941; *J.*, **1937**, 1865; 1939, 1177; *Discuss. Faraday Soc.*, 1950, **9**, 70; Burawoy and Spinner, *J.*, 1955, 2557; cf. also Gillam and Stern, "Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold and Co., London, 1954, p. 111).

Although the characteristic long-wave benzenoid bands observed in the spectra of benzene and many aromatic compounds possess lower intensities (ε generally less than 5000) and superficially appear to obey different rules, they originate in electronic transitions of the same type as those responsible for the *K*-bands (cf. below). Following a suggestion by Braude (*Ann. Reports*, **1945**, **42**, 105) these bands will be referred to as *B*-bands.

We have examined the electronic spectra of 2-nitrosoanisole, 6-methoxyiminocyclohexa-2 : 4-dienone (*o*-benzoquinone 1-monoxime methyl ether), and a few of their derivatives, since the qualitative understanding of these was required for the investigation of the structure of 2-nitrosophenols to be discussed in Part III (following paper).

The spectrum of nitrosobenzene (Fig. 1) in ethyl alcohol shows two types of absorption band above 2200 Å: (i) A *K*-band system of comparatively high intensity, consisting of two peaks at 2815 and 3055 Å (ε 9500 and 7000, respectively), which originates in a transition involving an electron migration along the conjugated system as indicated in (I) and corresponds to the benzene band at 2000 Å and the weak ethylene band system in the 1700 Å region. (ii) An *R*-band of low intensity at 7560 Å (ε 45), characteristic of the nitroso-group. The band corresponding to the 2600 Å band system of benzene is not observed since it is masked by the *K*-band absorption of higher intensity.



K-Bands.—The *K*-band of nitrosobenzene is displaced to longer wave-lengths in the spectra of 4-nitrosoanisole and *NN*-dimethyl-4-nitrosoaniline (Table 1). A similar red-shift of the *K*-band is observed in the series, 2-nitrosoanisole, 2 : 4-dimethoxy-1-nitrosobenzene, and 5-dimethylamino-2-nitrosoanisole (cf. Fig. 1 and Table 1). The methoxy- and dimethylamino-groups in the *para*-position to the nitroso-group are terminal groups of the absorbing conjugated system (I or II) and thus increase the polarity of the system as well as its length, *i.e.*, the electronic polarisability of the terminal group (cf. Burawoy and Spinner, *loc. cit.*). In contrast, a methoxy-group *ortho* to the nitroso-group, *i.e.*, in a branch of the absorbing conjugated system, does not increase the length of the system and modifies only slightly its polarity and thus has a smaller (bathochromic) effect on the *K*-band (for the spectra of nitrosobenzene and 2-nitrosoanisole, see Fig. 1, and for the data of all three investigated pairs of compounds, see Table 1).

* Part I, *J.*, 1952, 4793.

B-Bands.—In contrast to the *K*-band, the (masked) *B*-band of nitrosobenzene is strongly displaced to longer wavelengths, with an increased intensity, by an *ortho*-methoxy-group. It appears in the spectrum of 2-nitrosoanisole at 3770 Å (ε 4800), but remains

TABLE 1. *Spectra of nitrosobenzene derivatives, in ethanol.*

Compound	*R*-Band $\lambda_{max.}$ (Å)	*R*-Band ε	*B*-Band $\lambda_{max.}$ (Å)	*B*-Band ε	*K*-Band $\lambda_{max.}$ (Å)	*K*-Band ε
$C_6H_5\cdot NO$	7560	45	—	—	2815	9500
					3055	7000
1 : 2-MeO·$C_6H_4\cdot NO$	7610	41	3770	4800	2880	6900
					3090	5600
1 : 4-MeO·$C_6H_4\cdot NO$	7275	47	—	—	3455	11,600
2 : 4 : 1-$(MeO)_2C_6H_3\cdot NO$	7250	48	—	—	3690	12,100
1 : 4-$Me_2N\cdot C_6H_4\cdot NO$	6740	55	—	—	4200	30,400
2 : 4 : 1-MeO·$C_6H_3(NMe_2)\cdot NO$	6560	62	—	—	4210	33,800

masked in the spectra of 5-methoxy- and 5-dimethylamino-2-nitrosoanisole because of the red-shift of the *K*-band caused by the *para*-substituent. Moreover, a comparison of the spectra of 2-nitrosoanisole and its 5-methoxy-derivative (Fig. 1) shows that a *para*-

FIG. 1. FIG. 2.

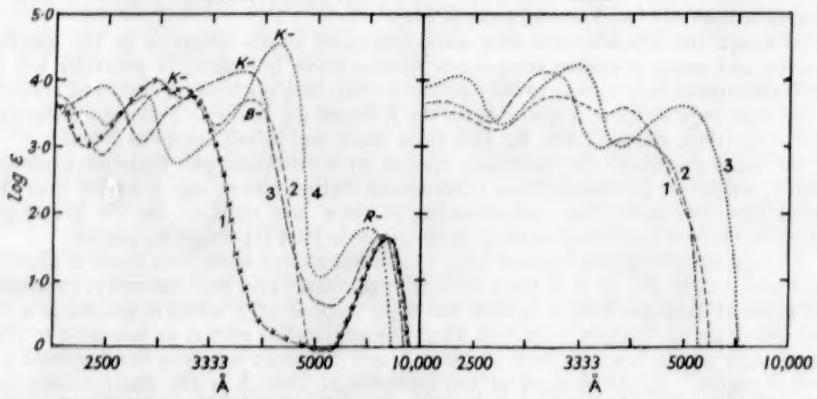


FIG. 1. 1, *Nitrobenzene*. 2, 2-*Nitrosoanisole*. 3, 2 : 4-*Dimethoxy*-1-*nitrosobenzene*. 4, 5-*Dimethylamino*-2-*nitrosoanisole*. In ethanol.

FIG. 2. 1, 6-*Methoxyimino*cyclo*hexa*-2 : 4-*dienone*. 2, 3-*Methoxy*-6-*methoxyimino*cyclo*hexa*-2 : 4-*dienone*. 3, 3-*Dimethylamino*-6-*methoxyimino*cyclo*hexa*-2 : 4-*dienone*. In ethanol.

methoxy-group can have only a small (probably hypsochromic) effect on the *B*-band. This reversed effect on the *K*- and *B*-bands, respectively, of a methoxy-group in *ortho* and the *para*-position to the nitroso-group is most characteristic and is also observed in the spectra of the corresponding hydroxy-derivatives of azobenzene, nitrobenzene, benzaldehyde, and diphenyl (for data, cf. Burawoy and Chamberlain, *J.*, 1952, 2310, 3734). Substituents

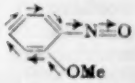
TABLE 2. *Spectra of nitrobenzenes*, $X\cdot C_6H_4\cdot NO_2$, *in ethanol.*

X		H	2-NH_2	4-NH_2	2-OH	4-OH	2-SH	4-SH
B-Band	$\lambda_{max.}$ (Å) ...	—	4030	—	3435	—	3540	—
	ε	—	6100	—	3600	—	3700	—
K-Band	$\lambda_{max.}$ (Å)	2595	2777	3725	2730	3140	2705	3175
	ε	9500	4900	16,800	6600	13,000	5700	24,000

such as amino and mercapto behave similarly, as shown in Table 2 by the spectra of the corresponding nitrobenzene derivatives.

These observations throw light on the nature of the electronic transition responsible

for the *B*-bands; they suggest that the *B*-bands originate in the same type of electronic transition as the *K*-bands, but correspond to electronic migrations along the conjugated system formed by all three benzene double bonds as indicated for benzene and 2-nitrosoanisole in formulæ (III) and (IV). Substituents such as hydroxy, amino, and mercapto

(III)  (IV)

ortho to double-bond groups are now terminal groups of the absorbing system and responsible for appreciable red-shifts, whereas in the *para*-position they are in a side-chain and have much smaller effects. Moreover, since the transition moment is much smaller, or even negligible, the lower intensities of the *B*-bands compared with those of the *K*-bands are also accounted for. This qualitative interpretation will be extended by a more detailed and fundamental discussion elsewhere.

R-*Bands*.—The effect of the methoxy- and the dimethylamino-group on the *R*-band of the nitroso-group is again different. The band is displaced to shorter wavelengths by the introduction of these groups in the *para*-position, the more strongly electron-repelling dimethylamino-group causing the greater blue-shift. The effect of an *ortho*-methoxy-group is small, a slight red-shift being observed in 2-nitrosoanisole (cf. Fig 1 and Table 1), very little change in 2 : 4-dimethoxy-1-nitrosobenzene, and a moderate blue-shift in 5-dimethylamino-2-nitrosoanisole (cf. Table 1). As already shown (Burawoy, *loc. cit.*, 1939), direct substitution of the nitroso-group by these substituents, *e.g.*, in the yellowish alkyl nitrites (λ 3570 Å; ε 75) and dimethylnitrosamine (λ 3435 Å; ε 97), is responsible for even greater displacements of the *R*-band to shorter wavelengths. As far as investigated, these effects are characteristic of the *R*-bands of all double bonds, *e.g.*, those of the N:N, C:S, and C:O groups (Burawoy, *locc. cit.*, 1930, 1937, 1939).

Solvent Effect.—Data showing the effect of solvents on the spectra of nitrosobenzene (I; X = H) and of 2-nitrosoanisole (II; X = H) and its 5-methoxy- (II; X = OMe) and 5-dimethylamino-derivatives (II ; X = NMe_2) are summarised in Table 3. This effect is undoubtedly complex, being dependent on the nature of the electronic transition (type of band) and the various possible solute–solvent interactions (for a discussion of the principles involved, cf. Bayliss and McRae, *J. Phys. Chem.*, 1954, **58**, 1002, 1006).

The data are in agreement with the following earlier conclusions (Burawoy, *locc. cit.*; in particular 1930, 1937, 1939, 1950) : (i) The *K*-bands (and *B*-bands) are displaced to longer, and the *R*-bands to shorter wavelengths approximately in the order of the increasing dielectric constant of the solvent : $C_6H_{14} < CCl_4 \sim Et_2O < C_6H_6 < CHCl_3 \sim EtOH < H_2O$. This is due mainly to the increasing polarity of the absorbing system in the ground state. The polarisability of the solvent (as indicated by its refractive index alone), the importance of which has been emphasised by Bayliss and his collaborators (*loc. cit.*, cf. also *J. Chem. Phys.*, 1950, **18**, 292), should make a smaller contribution in the case of the polar molecules and simple solvents investigated. The different effect of solvents on *R*- and *K*-bands (interpreted to correspond to $n \longrightarrow \pi$ and $\pi \longrightarrow \pi$ transitions) has been recently discussed by McConnell (*J. Chem. Phys.*, 1952, **20**, 700). (ii) The increase in the polarity due to the solute–solvent interaction, and thus the magnitude of the solvent effect is enhanced with the polar character of the absorbing molecules. It is small for nitrosobenzene and 2-nitrosoanisole, moderate for the 5-methoxy-derivative, and appreciable for 5-dimethylamino-2-nitrosoanisole.

Whereas the *K*-bands are usually at the longest wavelengths in water, that of *NN*-dimethyl-3-methoxy-4-nitrosoaniline (II; X = NMe_2) appears at shorter wavelengths (4160 Å) in this solvent than in chloroform (4180 Å) and ethanol (4210 Å). This partial reversal of the normal solvent effect may be attributed to the formation of an external hydrogen bond by the dimethylamino-group. This is similar to the behaviour of dimethylaniline itself as explained by Ungnade (*J. Amer. Chem. Soc.*, 1953, **75**, 432). Both the *B*- and *K*-bands of dimethylaniline are displaced to shorter wavelengths in passing from *cyclo*hexane or ethyl alcohol (λ 2980 and 2510 Å respectively; log ε 3·37 and 4·16) to water

(λ 2840 and 2440 Å; log ε 3·11 and 3·94). This effect is too big to be attributed to the smaller polarisability of water, as suggested by Bayliss and McCrae (*loc. cit.*).

TABLE 3. *Effect of solvents on the spectra of nitrosobenzenes* (I *and* II).

		(I; X = H)		(II; X = H)		(II; X = OMe)		(II; X = NMe_2)	
Solvent	Band	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
C_6H_{14}	*R*	7660	45	—	—	—	—	—	—
	K	2800	11,900	—	—	—	—	—	—
		3025	5900						
Et_2O	*R*	7625	44	7770	46	7525	50	—	—
	B	—	—	3715	4950	—	—	—	—
	K	2810	7650	2870	6900	3610	11,250	4000	30,300
		3035	4900	3060 *	3700				
CCl_4	*R*	—	—	7770	53	—	—	7340	68
	B	—	—	3690	4850	—	—	—	—
	K	—	—	2890	5750	3605	11,200	4015	30,200
				3040 *	3750				
C_6H_6	*R*	7640	48	7760	54	7475	59	7310	72
	B	—	—	3755	4600	—	—	—	—
	K	2835	9250	2895	6300	3660	10,800	4070	28,700
		3070	7800	3060 *	4300				
$CHCl_3$ ...	*R*	7550	48	7660	49	7360	56	7080	76
	B	—	—	3800	4800	—	—	—	—
	K	2835	11,800	2890	6600	3710	12,100	4180	35,000
		3055	10,600	3090	5400				
EtOH ...	*R*	7560	45	7610	41	7250	48	6560	62
	B	—	—	3770	4800	—	—	—	—
	K	2815	9500	2880	6900	3690	12,100	4210	33,800
		3055	7000	3090	5600				
H_2O	*R*	7310	29	7440 †	23	6990 †	54	5450 *	123
	B	—	—	3910	2700	—	—	—	—
	K	2825	6250	2860	5300	3740	12,200	4160	28,500
		3065	8500	3120	5650				
D ‡	*R*	− 65 Å		−160		−275		− 780	
		−120 $cm.^{-1}$		−270		−500		−1620	
	B	—		+ 55		—		—	
				+400					
	K	+ 10 Å		+ 20		+ 80		+ 210	
		+130 $cm.^{-1}$		+250		+600		+1250	

* Inflexion. † Ethanol–water (1 : 1).

‡ Displacement $D(Et_2O \longrightarrow EtOH)$, except for *R*-band in (II; X = NMe_2), which is $D(CCl_4 \longrightarrow EtOH)$.

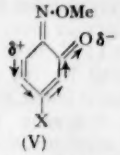
6-*Methoxyimino*cyclo*hexa*-2 : 4-*dienones* (o-*Benzoquinone* 1-*Oxime Methyl Ethers*).—A detailed and unambiguous analysis of the spectra of 6-methoxyimino*cyclo*hexa-2 : 4-dienone (V; X = H) and its 3-methoxy- (V; X = OMe) and 3-dimethylamino-derivatives (V; X = NMe_2) (for data, cf. Fig. 2 and Table 4) would require an extensive knowledge of the *o*-benzoquinone system and will not be attempted. The following observations can, however, be made.

The spectra above 2500 Å of the three compounds in all solvents consist of two band systems, of which that at longer wavelengths possesses a lower intensity. No *R*-band is observed since the nitroso-group is absent and that of the carbonyl group masked by the more intense bands. The band system at shorter wavelengths (a *K*-band) of the parent compound in ethanol has one peak at 3070 Å (ε 5500) and an inflexion at 3350 Å (ε 4400). It is very similar to the *K*-band system of the isomeric 2-nitrosoanisole in ethanol (λ 2880 and 3090 Å; ε 6900 and 5600) in spite of the very different structures of the two compounds.

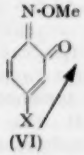
The corresponding *K*-bands of the 3-methoxy- and 3-dimethylamino-derivatives in ethanol consist of only one peak of higher intensity, but, in contrast to the isomeric 2-nitrosoanisoles, the introduction of these groups has only a small effect on the position of the peak, the methoxy-group displacing to shorter and the dimethylamino-group to longer wavelengths (−60 and +220 Å, respectively). Since these groups behave as if

present in a side-chain of the absorbing (conjugated) system, the electron transition may involve an electron migration as indicated in (V).

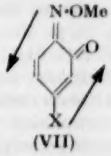
Again, both the intensity and position of the long-wave band in the spectrum of the parent methoxyimino*cyclo*hexadienone (λ 3780 Å; ε 3800) and of the *B*-band in the spectrum of 2-nitrosoanisole (λ 3770 Å; ε 4800) are very similar. However, in contrast to 5-methoxy- and 5-dimethylamino-2-nitrosoanisole, this band appears in the spectra of the 3-methoxy- and 3-dimethylamino-6-methoxyimino*cyclo*hexadienone at 4010 and 4890 Å, respectively (in ethanol), *i.e.*, red-shifts of 230 and 1110 Å being observed. This allows little doubt that the methoxy- and dimethylamino-groups are terminal groups of the absorbing conjugated system and indicates the electronic transition shown in (VI).



(V)



(VI)



(VII)

This would not account for the only moderate intensities (ε 1550 and 4000, respectively) which correspond to those of *B*-bands. It may, therefore, be suggested that the electron migration involved in the transition is coupled with one in the opposite direction as indicated in (VII), resulting in the small transition moment characteristic of *B*-bands.

Data for the effect of solvents on the bands of all three methoxyimino*cyclo*hexadienones are summarised in Table 4. As in the case of the *B*- and the *K*-bands of the 2-nitroso-

TABLE 4. *Effect of solvents on the spectra of* 6-*methoxyimino*cyclo*hexa*-2 : 4-*dienones* (V).

		(V; X = H)		(V; X = OMe)		(V; X = NMe_2)	
Solvent	Band	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
Et_2O	*B*	3750	3600	3760	1950	4700	2600
	K	3030	4800	2940	13,300	3160	14,700
		3320 *	3700			3290	13,600
CCl_4	*B*	3700	4000	3880	2300	4770	2750
	K	3050	4300	2985	16,600	3215	14,100
		3350	4000				
C_6H_6	*B*	3740	4000	3920	1700	4810	3100
	K	3060	5050	3010	15,400	3235	16,400
		3350	4100				
$CHCl_3$	*B*	3830	3200	3960	1750	4890	3750
	K	3060	4750	3010	12,200	3275	16,300
		3350 *	3400				
EtOH	*B*	3780	3750	4010	1550	4890	4000
	K	3070	5550	3010	14,900	3290	16,700
		3325 *	4400				
H_2O	*B*	3910	3000	4110	1750	4830	5000
	K	3080	5600	3060	13,200	3310	18,900
		3350 *	4400				
D †	*B*	+30 Å		+250		+190	
	K	+25		+ 70		+ 65	

* Inflexion. † *D*(Et_2O ⟶ EtOH).

anisoles, moderate red-shifts, approximately in the order of solvents, $Et_2O \sim CCl_4 < C_6H_6 < CHCl_3 \sim EtOH < H_2O$, are observed, the displacements being smallest in the case of the least polar parent methoxyimino*cyclo*hexadienone. Again, the formation of an external hydrogen bond with water should account for the blue-shift of the *B*-band and rather small red-shift of the *K*-band of the 3-dimethylamino-derivative in this solvent as compared with their positions in chloroform and ethanol.

EXPERIMENTAL

Spectra of the nitroso-compounds and 6-methoxyimino*cyclo*hexadienones were determined with a Hilger Uvispek Photoelectric Spectrophotometer. The concentrations used varied

between 0·01M and 0·0025M for the *R*-bands and between 0·0001M and 0·0004M for the *B*- and *K*-bands. The data for the nitrobenzene derivatives (Table 2) are new determinations carried out with a Hilger E3 quartz spectrograph fitted with a Spekker photometer, a tungsten-steel high-tension spark being employed as the source of light; those for nitrobenzene and the nitrophenols have already been reported (Burawoy and Chamberlain, *loc. cit.*).

Materials.—*2-Nitrosoanisole.* This formed white plates (from water), m. p. 103° (Baeyer and Knorr, *Ber.*, 1902, **35**, 3036, give m. p. 103°).

6-Methoxyiminocyclohexa-2 : 4-dienone. Aqueous silver nitrate (3·5 g. in 20 c.c.) was added to aqueous sodium 2-nitrosophenoxide (Baeyer and Knorr, *loc. cit.*; 3 g. in 20 c.c.), and the silver 2-nitrosophenoxide filtered off. Methyl iodide (10 g.) was shaken with a suspension of the dry silver salt in dry ether (200 c.c.) for 50 hr., the resulting ethereal solution filtered, the ether removed under reduced pressure, and the residue (1 g.; 35%) crystallised from light petroleum (b. p. 40—60°). The *methoxyiminocyclohexadienone* formed orange needles, m. p. 48° (Found: C, 61·1; H, 4·8; N, 10·2. $C_7H_7O_2N$ requires C, 61·3; H, 5·1; N, 10·2%).

2 : 4-Dimethoxy-1-nitrosobenzene. Attempts to prepare this compound by the action of sodium nitrite on resorcinol dimethyl ether in presence of aqueous mineral acid failed, nitrosation being accompanied by demethylation. It was obtained by the following methods: (i) Potassium persulphate (5·7 g.) was gradually added to concentrated sulphuric acid (9 c.c.) with stirring, the temperature being kept below 15°. The mixture was stirred for another 45 min. and then poured on ice (200 g.). The solution was neutralised with potassium carbonate and finally made slightly acidic with dilute acetic acid, the temperature being kept at 0—5°. 2 : 4-Dimethoxyanilinium chloride (1·8 g.) in water (150 c.c.) was neutralised with sodium hydroxide and slightly acidified with dilute acetic acid. The solution of Caro's acid was added at once, the temperature being kept below 5°. After 30 min., salt was added and the precipitate collected and steam-distilled. *2 : 4-Dimethoxy-1-nitrosobenzene* (0·6 g., 45%) was again salted out and crystallised from water or light petroleum, forming green needles, m. p. 98—99° (Found: C, 57·6; H, 5·5; N, 8·6. $C_8H_9O_3N$ requires C, 57·5; H, 5·4; N, 8·4%). (ii) Sodium nitrite (6·9 g.) was added slowly to concentrated sulphuric acid (69 c.c.) with stirring and cooling below 10°. The temperature was slowly raised to 65°, a clear solution being obtained. Resorcinol dimethyl ether (4·6 g.) was added dropwise, the temperature being maintained below 5°; stirring was continued for another 15 min. and the mixture poured on to ice water and sodium carbonate. The precipitate (4·1 g., 73%) was crystallised from light petroleum, giving green needles, m. p. 98—99°, identical with the product obtained from dimethoxyanilinium chloride.

3-Methoxy-6-methoxyiminocyclohexa-2 : 4-dienone. This formed orange spears (from light petroleum), m. p. 115—116° (Henrich and Eisenach, *J. praht. Chem.*, 1904, **70**, 332, give m. p. 115—117°).

5-Dimethylamino-2-nitrosoanisole. This was obtained as green needles (from carbon tetrachloride), m. p. 131° (Fieser and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 382, give 131°).

3-Dimethylamino-6-methoxyiminocyclohexa-2 : 4-dienone. Aqueous silver nitrate (6 g. in 30 c.c.) was added to 5-dimethylamino-2-nitrosophenol (5 g.) in water (180 c.c.) and sodium hydroxide (15 c.c.; 2N). The dried silver salt was shaken with methyl iodide (5 g.) in dry ether (350 c.c.) in a stoppered bottle for 48 hr. The solution was filtered, the ether removed and the *3-dimethylamino-6-methoxyiminocyclohexadienone* (4 g., 74%) crystallised from carbon tetrachloride, giving reddish-brown needles, m. p. 149°. The product is easily soluble in water and is very hygroscopic (Found: C, 59·6; H, 6·6; OMe, 17·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7; OMe, 17·2%).

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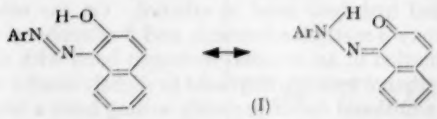
The Nature of the Internal Hydrogen Bond. Part III. Tautomeric Equilibria of 2-Nitrosophenols.*

By A. Burawoy, M. Cais, J. T. Chamberlain, F. Liversedge, and A. R. Thompson.

[Reprint Order No. 6385.]

The electronic spectra of 2-nitrosophenol, 5-methoxy-2-nitrosophenol, and 5-dimethylamino-2-nitrosophenol in various solvents are determined and compared with those of the corresponding 2-nitrosoanisoles and 6-methoxyimino*cyclo*hexa-2 : 4-dienones. It is shown that these compounds contain an internal hydrogen bond and that, in spite of it, the methoxy- and dimethylamino-derivatives exist as solvent-dependent tautomeric equilibria. This confirms that an internal hydrogen bond cannot be interpreted as a non-localised bond, such as in (I) or (II). In all solvents, the parent compound is observed only as the true 2-nitrosophenol tautomer. The participation of the nitroso-group in an internal hydrogen bond is responsible for a strong displacement of the *R*-band to shorter wavelengths (800—1200 Å).

An investigation of the electronic spectra of 1-phenylazo-2-naphthol and its derivatives in various solvents has established that these compounds exist as solvent-dependent tautomeric equilibria (Burawoy, Salem, and Thompson, *Chem. and Ind.*, 1952, 668; Part I *; Burawoy and Thompson, *J.*, 1953, 1443). This is conclusive evidence that an internal hydrogen bond, as present in both tautomers of these compounds, cannot be interpreted as a non-localised bond, *e.g.*, as a resonance hybrid such as (I).

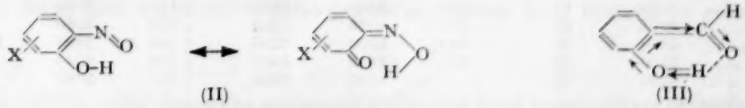


(I)

Simultaneously, we have carried out an examination of the electronic spectra of 2-nitrosophenol, 5-methoxy-2-nitrosophenol, and 5-dimethylamino-2-nitrosophenol in various solvents, in order to ascertain whether these compounds exist as true nitroso-compounds, as *o*-benzoquinone monoximes, as tautomeric equilibria, or as resonance hybrids such as (II).

The ability of 2-nitrosophenols to form stable complex salts, which have application in inorganic analysis and as colouring matters, already indicates that they contain an internal hydrogen bond, but an additional aim of this investigation has been to obtain direct spectroscopic evidence for its presence and, possibly, to obtain information of the effect of this bond on the *R*-band (of the nitroso-group).

It has already been shown (Morton and Stubbs, *J.*, 1940, 1347; Burawoy and Chamberlain, *J.*, 1952, 2310, 3734) that an internal hydrogen bond displaces the *B*- and the *K*-bands



(II) (III)

of phenols to longer wavelengths, undoubtedly because the polarity of the absorbing system (in the ground state) is increased by polarisation (cf. III). Thus, these bands in the spectra in hexane of 4-hydroxydiphenyl, 2-hydroxydiphenyl, 3-methoxybenzaldehyde, and 4-hydroxyazobenzene appear at slightly shorter wavelengths than in the spectra of the corresponding methyl ethers, whereas those of salicylaldehyde, which

* Parts I and II, *J.*, 1952, 4793; preceding paper.

contains an internal hydrogen bond, are observed (in hexane) at longer wavelengths than the corresponding bands of 2-methoxybenzaldehyde (for data see Table 1). This is also true for 2-hydroxy-5-methylazobenzene and 2-nitrophenol, but in these examples the blue-shift of the *B*- and *K*-bands of the corresponding methyl ethers is considerably greater, being enhanced by the intramolecular steric interaction between the methoxy-group and the azo- and nitro-group, respectively.

An additional and, for the following discussion, important criterion for the presence of an internal hydrogen bond is the characteristic effect of solvents. The *B*- and *K*-bands of the former phenols are displaced to longer wavelengths approximately as the dielectric constant of the solvent increases. This is shown in Table 1 for hexane and ethanolic

TABLE 1. *B- and K-Bands of phenols and their methyl ethers.**

	Phenol								Methyl ether			
	In hexane				In ethanol				In hexane			
	B-Band		*K*-Band		*B*-Band		*K*-Band		*B*-Band		*K*-Band	
	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
1 : 4-$C_6H_5{\cdot}C_6H_4{\cdot}OH$	—	—	2558	25,000	—	—	2612	22,500	—	—	2596	27,000
1 : 2-$C_6H_5{\cdot}C_6H_4{\cdot}OH$	2825	5750	2442	12,500	2880	5500	2470	13,500	2835	6200	2460	15,500
1 : 3-HO-$C_6H_4{\cdot}CHO$	3050	2700	2480	12,000	3155	3000	2537	9500	3050	3000	2488	10,000
1 : 4-$C_6H_5{\cdot}N{:}N{\cdot}C_6H_4{\cdot}OH$	—	—	3365	28,500	—	—	3510	29,000	—	—	3380	24,700
1 : 2-HO-$C_6H_4{\cdot}CHO$	3285	3230	2550	10,000	3250	3000	2550	10,000	3100	5620	2465	12,000
1 : 5 : 2-$C_6H_5{\cdot}N{:}N{\cdot}C_6H_3Me{\cdot}OH$	3935	9800	3230	25,000	3935	9600	3235	25,000	3590	9000	3090	13,500
1 : 2-HO-$C_6H_4{\cdot}NO_2$	3460	3900	2710	7600	3435	3600	2730	6600	3172†	2850	2585	3450

* Cf. Burawoy and Chamberlain, *loc. cit.* † In ethanol.

solutions and is due mainly to the increasing polarity of the absorbing system resulting partly from the dielectric effect of the solvent and partly from the formation of a true (stoicheiometric) external hydrogen bond in ethanol. On the other hand, the bands of salicylaldehyde, 2-hydroxy-5-methylazobenzene, and 2-nitrophenol are almost unchanged, partly because the formation of an external hydrogen bond with the solvent is inhibited. Some of these bands in ethanol are even displaced to slightly shorter wavelengths, indicating the contribution of an additional factor probably arising from a weakening of the internal hydrogen bond in solvents of higher dielectric constant.

No investigation of the effect of an internal hydrogen bond on *R*-bands has been reported. These bands, in contrast to *B*- and *K*-bands, are known to be displaced to *shorter* wavelengths by influences (substituents, solvents, proton addition) increasing the polarity of the chromophoric double bonds (for references, cf. Part II, *loc. cit.*). It would, therefore, be expected that the participation of the groups in an internal hydrogen bond would show a similar effect.

TABLE 2. *Spectra of 2-nitrosophenol.*

	R-Band			*B*-Band			*K*-Band *	
Solvent	$\lambda_{max.}$	ε	*D* †	$\lambda_{max.}$	ε	*D* †	$\lambda_{max.}$	ε
C_6H_{14}	6975	47	—	3950	2000	—	2995	8200
CCl_4	6975	65	−795	4000	2600	+310	3000	10,900
Et_2O	7025	44	−745	3910	2650	+195	3020	8900
C_6H_6	6975	60	−785	4025	2200	+270	3060	8700
$CHCl_3$	6850	55	−810	4060	2250	+260	3060	10,900
EtOH	7150	53	−460	3890	3400	+120	3040	7800
H_2O	6730	31	—	3990	2300	+80	3080	6300

* Owing to fine structure of the *K*-band of 2-nitrosoanisole, no accurate values of *D*(Me ⟶ H) can be given.

† *D* refers to *D*(Me ⟶ H) in all cases, measured in Å.

2-Nitrosophenol.—Data for the spectra of 2-nitrosophenol in various solvents and the displacements [*D*(Me ⟶ H)] of the *R*- and *B*-bands as compared with the corresponding bands of 2-nitrosoanisole are shown in Table 2. The spectra in hexane and ethanol together with those of 2-nitrosoanisole and 6-methoxyimino*cyclo*hexa-2 : 4-dienone in ethanol

are reproduced in Fig. 1. In all solvents, 2-nitrosophenol exhibits the characteristic *R*-band of the nitroso-grcup (λ 6730—7150 Å; ε 31—65), thus establishing the presence of this compound in solution as a true nitroso-compound. The *R*-band is observed in all solvents at considerably shorter wavelengths than that of 2-nitrosoanisole (λ 7440—7770 Å; ε 23—54) and, in contrast to the normal effect of solvents as, *e.g.*, shown by 2-nitrosoanisole (cf. Part II), appears at the longest wavelength in ethanol. These facts afford experimental evidence for the presence of an internal hydrogen bond in 2-nitrosophenol and show that this bond is responsible for a considerable blue-shift of the *R*-band (700—800 Å) which is comparable with the opposite one observed for *B*- and *K*-bands, *e.g.*, of salicylaldehyde (cf. Table 1) and of 2-nitrosophenol itself (cf. Table 2).

As shown in Part II, the ultraviolet spectra of 2-nitrosoanisole and 6-methoxyimino-*cyclo*hexa-2 : 4-dienone (consisting of *B*- and *K*-bands) are surprisingly similar, but, fortunately, the *K*-band system of the methoxyimino-compound is displaced by approximately

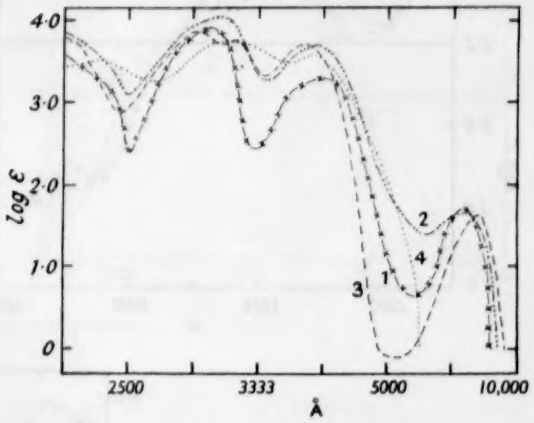
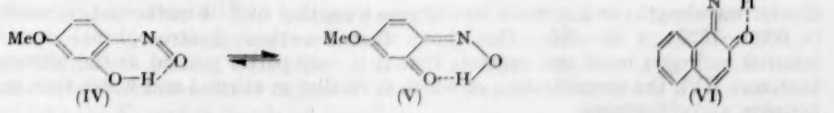


FIG. 1.

1, 2-*Nitrosophenol in hexane.*
2, 2-*Nitrosophenol in ethanol.*
3, 2-*Nitrosoanisole in ethanol.*
4, 6-*Methoxyiminocyclohexa*-2 : 4-*dienone in ethanol.*

200 Å to longer wavelengths. The *K*-band of 2-nitrosophenol, which in contrast to that of the ethers consists of only one peak of greater intensity, has in all solvents an intermediate position (cf. *e.g.*, Fig. 1 for the spectra in ethanol). Since the methylation of a hydroxy-group participating in an internal hydrogen bond displaces a *K*-band to shorter wavelengths, this band must be attributed to the true nitrosophenol tautomer. The presence of an internal hydrogen bond is supported by the red-shift of the *B*-band in all solvents (λ 80—310 Å) as compared with the *B*-band of 2-nitrosoanisole (as well as of the methoxyimino*cyclo*hexadienone) and by the characteristic blue-shift of its maximum in ethanol (and water). The electronic spectra show that 2-nitrosophenol exists in solution as the true nitrosophenol tautomer, although they cannot exclude the presence of small, but undetectable, amounts of the oxime tautomer.

5-Methoxy-2-nitrosophenol.—Henrich and Eisenach (*J. prakt. Chem.*, 1904, **70**, 332) have shown that 5-methoxy-2-nitrosophenol crystallises from benzene as green dichroic



prisms and from ethanol as yellowish-brown prisms. The former changed into the brown form below the melting point. They suggested that these two forms represent the 2-nitrosophenol and *o*-quinone oxime tautomers (IV and V), respectively. We have confirmed these observations and found that in solution both forms give an identical spectrum.

Powder photographs of the solid forms taken by Dr. G. W. R. Bartindale reveal very different *X*-ray patterns. Data of the spectra in various solvents are collected in Table 3, and a few diagrams are reproduced with those of 2 : 4-dimethoxy-1-nitrosobenzene and 3-methoxy-6-methoxyimino*cyclo*hexa-2 : 4-dienone in ethanol in Figs. 2 and 3.

The spectra of 5-methoxy-2-nitrosophenol exhibit in all solvents the characteristic *R*-band of the nitroso-group (λ 6100—6460; ε 10—35), but it always appears at appreciably

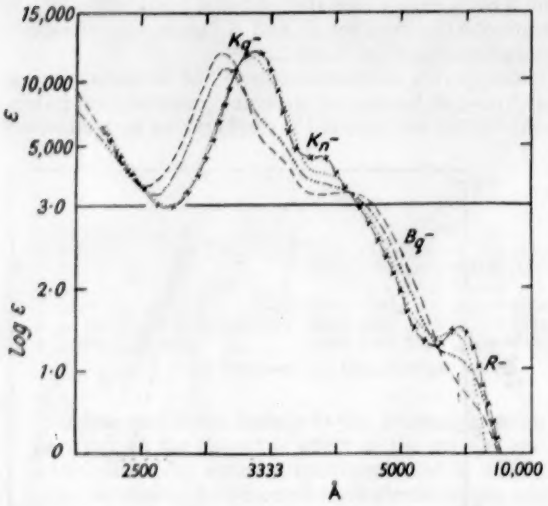


FIG. 2. *5-Methoxy-2-nitrosophenol in*
— × — × — *ethyl ether.*
. . . . . *chloroform.*
— . — . — *ethanol.*
— — — — — *water.*

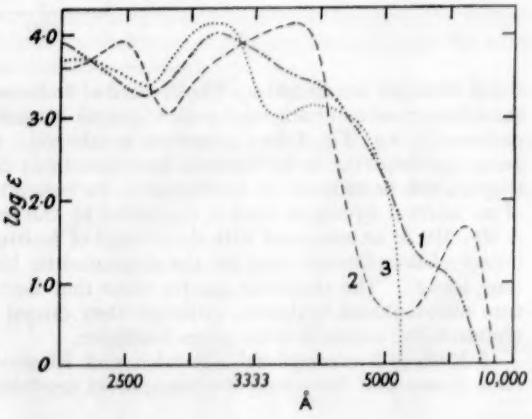


FIG. 3.
1, *5-Methoxy-2-nitrosophenol.*
2, 2 : 4-*Dimethoxy-1-nitrosobenzene.*
3, 6-*Methoxyimino*cyclo*hexa*-2 : 4-*dienone. In ethanol.*

shorter wavelengths and is much less intense than that of 2 : 4-methoxy-1-nitrosobenzene (λ 6990—7525; ε 48—59). This shows that 5-methoxy-2-nitrosophenol contains an internal hydrogen bond and suggests that it is only partly present as the nitrosophenol tautomer (IV), the concentration of which is smaller in ethanol and water than in ether, benzene, and chloroform.

This interpretation is supported by the appearance of a band or inflexion at about 3750 Å (ε <4400) which can only correspond to the *K*-band appearing in 2 : 4-dimethoxy-1-nitrosobenzene at slightly shorter wavelengths (λ 3600—3740 Å; ε 11,000—12,000), *i.e.*, it is due to the *K*-band of the nitrosophenol tautomer (K_n). Again, its intensity in

all solvents is appreciably lower than that of the anisole and decreases approximately in the same order of solvents as does the *R*-band due to the nitroso-group.

This band (or inflexion) cannot be due to the *B*-band of the 4-methoxy-*o*-quinone 1-oxime tautomer (B_q). The latter would be expected to be at longer wavelengths and of lower intensity than that of the methoxyimino-compound (λ 3760—4110 Å; ε <2000), just as the *B*-bands of salicylaldehyde and 2-nitrosophenol lie at longer wavelengths and

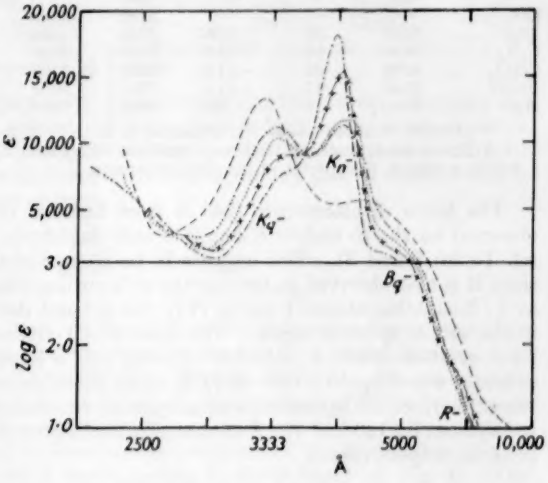


FIG. 4.

5-Dimethylamino-2-nitrosophenol in
— · — · — · — *carbon tetrachloride.*
. . . . . *chloroform.*
— — — — — *water.*
— × — × — *benzene.*
— · · · — · · · — *ethanol.*

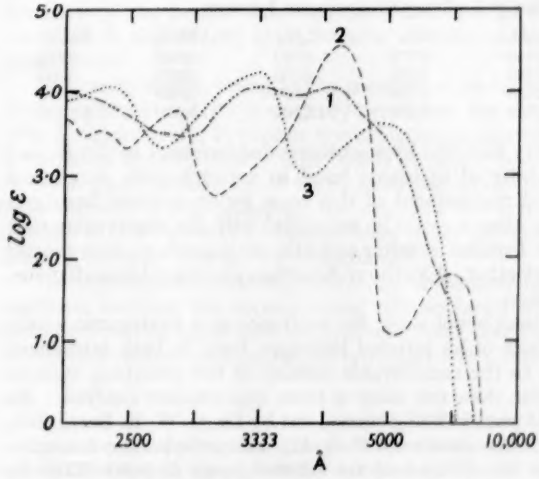


FIG. 5.

1, *5-Dimethylamino-2-nitrosophenol.*
2, *5-Dimethylamino-2-nitrosoanisole.*
3, *3-Dimethylamino-6-methoxyimino-cyclohexa-2:4-dienone.* In ethanol.

are less intense than those of their methyl ethers (cf. Table 1 and Fig. 1, respectively). It is, indeed, observed as an inflexion superposed on the red slope of the K_n-band at about 3750 Å, its intensity increasing from ether to water, *i.e.*, in the opposite order of solvents. This results in a broad absorption region at 4000 Å in water which is due to the superposition of both the K_n- and B_q-bands (cf. Fig. 2).

The presence of the *o*-quinone oxime tautomer is unambiguously confirmed by the appearance in all solvents of its expected *K*-band (K_q) in the region 2960—3230 Å (ε 11,000—12,300) which corresponds to the *K*-band of the 3-methoxy-6-methoxyimino*cyclo*hexadienone at 2940—3060 Å (ε 12,200—16,600). An internal hydrogen bond is indicated by

the appreciable red-shift in non-hydroxylic solvents as compared with the methyl ether and by the characteristic blue-shift approximately following the order of increasing dielectric constant of the solvent (cf. Table 3).

TABLE 3. *Spectra of 5-methoxy-2-nitrosophenol.*

	R-Band			K_a-Band			K_ϕ-Band		
Solvent	$\lambda_{max.}$	ε	*D* *	$\lambda_{max.}$	ε	*D* *	$\lambda_{max.}$	ε	*D* *
CCl_4	—	—	—	3750	4000	+145	3225	12,300	+240
Et_2O	6460	32	−1065	3740	4400	+130	3225	11,900	+285
C_6H_6	6430	35	−1045	3750 †	3800	+ 90	3230	11,600	+220
$CHCl_3$ ...	6220	29	−1140	3750 †	3500	+ 40	3175	12,100	+165
EtOH ...	6140	15	−1110	3700 †	3050	+ 10	2990	11,000	− 20
H_2O	6100 ‡	10	− 890	4000 §	2050	—	2960	12,000	−100

* *D* refers to *D*(Me ⟶ H), measured in Å. † Inflexion. ‡ Ethanol–water (1 : 1).
§ Broad band resulting from superposition of K_a- and B_ϕ-bands, the latter appearing as a steep inflexion also in the spectra of the other solutions.

The latter displacements (240 Å from benzene to ethanol) are greater than those observed for the *B*- and/or *K*-bands of salicylaldehyde, 2-nitrophenol, and 2-nitrosophenol (cf. Tables 1 and 2). This appears to be characteristic of the *o*-quinone oxime system, since it is also observed in the spectra of 1-nitroso-2-naphthol which exists in all solvents as 1 : 2-naphthaquinone 1-oxime (VI), the *R*-band due to the nitroso-group being absent in the visible spectral region. The spectra of 1-nitroso-2-naphthol show a high-intensity band at 2630—2800 Å (ε 10,800—13,500) and a band of lower intensity (ε 5000—6000) at longer wavelengths (3725—3820 Å) which should be comparable with the *K*- and *B*-bands, respectively, of the benzenoid *o*-benzoquinone oximes (cf. Table 4). The *K*-band in ethanol is displaced by 110 and 170 Å to shorter wavelengths as compared with that in hexane and benzene, respectively.

TABLE 4. *Spectra of* 1 : 2-*naphthaquinone* 1-*oxime.*

		C_6H_{14}	Et_2O	CCl_4	C_6H_6	$CHCl_3$	EtOH
B-Band	$\lambda_{max.}$, Å	3750	3740	3775	3790	3820	3725
	ε	5700	5700	6000	5700	5800	5000
K-Band	$\lambda_{max.}$, Å	2740	2735	2755	2800	2745	2630
	ε	12,400	10,800	12,600	12,000	13,500	12,200

We have considered the possibility that the hypsochromic displacement of the *B*- and *K*-bands of phenols containing an internal hydrogen bond in solvents such as ethanol and water might be due to a partial replacement of this bond by an external hydrogen bond with the solvent, but this view cannot easily be reconciled with the observation that the *K*-band of 4-methoxy-*o*-quinone 1-oxime in water and ethanol appears at even shorter wavelengths than that of its methyl ether, 3-methoxy-6-methoxyimino*cyclo*hexadienone. This matter requires further elucidation.

The spectra of 5-methoxy-2-nitrosophenol show the existence of a tautomeric equilibrium in all solvents and the presence of an internal hydrogen bond in both tautomers. The complexity of the spectra due to the considerable overlap of the absorbing systems of the tautomers in the middle region does not allow a more quantitative analysis. An *X*-ray analysis of the solid forms is at present being carried out by Dr. G. W. R. Bartindale.

5-Dimethylamino-2-nitrosophenol.—As shown in Part II, 5-dimethylamino-2-nitrosoanisole in various solvents exhibits the *R*-band of the nitroso-group (λ 5450—7340 Å; ε 60—80) and a *K*-band (λ 4000—4210 Å; ε 28,000—35,000), whereas 3-dimethylamino-6-methoxyimino*cyclo*hexadienone exhibits a *B*-band (λ 4700—4900 Å; ε 2600—5000) and a *K*-band (λ 3200—3300 Å; ε 14,000—19,000). The spectra of 5-dimethylamino-2-nitrosophenol in all solvents show the presence of each of the four band systems, confirming its existence as a tautomeric equilibrium (VII ⇌ VIII). Data of spectra in various solvents are collected in Table 5. A few spectra are shown together with those of the two methyl ethers in ethanol in Figs. 4 and 5.

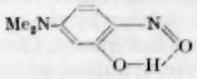
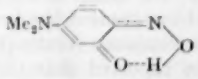
The *K*-bands (or inflexions) of the 2-nitrosophenol tautomer (VII) and the *o*-benzoquinone oxime tautomer (VIII) are observed at 3960—4100 Å (ε 5600—18,500) and at

TABLE 5. *Spectra of 5-dimethylamino-2-nitrosophenol.*

Solvent	B_q-Band * ε 5000 Å	K_n-Band $\lambda_{max.}$	K_n-Band ε	K_n-Band D †	K_q-Band $\lambda_{max.}$	K_q-Band ε	K_q-Band D †
CCl_4	780	3960	18,500	− 55	3400 *	7500	+185
Et_2O	1130	4000	17,300	− 0	3400 *	9200	+175
C_6H_6	1450	4035	15,400	− 35	3475	9000	+240
$CHCl_3$	1920	4080	11,800	−100	3360	10,300	+ 85
EtOH	2230	4040	11,400	−170	3340	11·100	+ 50
H_2O	3390	4225 ‡	5600	—	3245	13,400	− 65

* Inflexion. † D refers to D(Me ⟶ H), measured in Å.
‡ Broad band resulting from superposition by B_q-band.

3245—3475 Å (ε 7500—13,400), respectively. The intensity of the former decreases and that of the latter increases in the solvent order: carbon tetrachloride, ether, benzene, chloroform, ethanol, and water. Little importance can be attached to the small displacements of the maxima as compared with those of the corresponding methyl ethers owing to the considerable overlap of these band systems.

(VII)  ⇌  (VIII)

The B_q-band corresponding to that of the 3-dimethylamino-6-methoxyiminocyclohexa-2 : 4-dienone appears as an inflexion overlapping the red slope of the K_n-band. In aqueous solution, a very broad band at 4225 Å (ε 5600) is observed. Its considerable width is due to superposition of the B_q-band on the K_n-band, which in this solvent reach the highest and lowest intensity, respectively. In agreement with this interpretation, in all other solvents this broad band divides into its components, the K_n-band at 3960—4100 Å and an inflexion at about 5000 Å corresponding to the B_q-band (cf. Fig. 4). The intensity of the former band increases and that of the latter (similar to the K_q-band) decreases in the solvent order: water, alcohol, chloroform, benzene, ether, and carbon tetrachloride.

As already shown, owing to the presence of an internal hydrogen bond, the *R*-bands of 2-nitrosophenol and its 5-methoxy-derivative are displaced by approximately 800 and 1050 Å, respectively, to shorter wavelengths, compared with those of their methyl ethers. A similar or slightly greater shift could, therefore, be expected for the *R*-band of the 5-dimethylamino-2-nitrosophenol tautomer which would place the maximum in the region of 6000—6200 Å. This is indeed the case, but owing to the overlap with the more intense B_q-band in this region it is observed only as an inflexion which is particularly well defined in ether, benzene, and carbon tetrachloride.

The existence of 5-methoxy- and 5-dimethylamino-2-nitrosophenol as solvent-dependent equilibria between the corresponding nitrosophenol and quinone oxime tautomers, both tautomers containing an internal hydrogen bond, confirms that this bond is of an essentially electrostatic nature and cannot be interpreted as a non-localised bond.

EXPERIMENTAL

Spectra were determined with a Hilger Uvispek Photoelectric Spectrophotometer. The concentrations used varied between 0·005 and 0·03M for the *R*-bands and 0·0002 and 0·0005M for the *B*- and *K*-bands. In view of the difficulty of isolating the very volatile 2-nitrosophenol (cf. Baudisch, *Ber.*, 1912, **45**, 1164; 1915, **48**, 1660), its solutions were prepared by adding potassium hydrogen sulphate and a very small drop of distilled water to suspensions or solutions respectively of its sodium salt (cf. Part II), shaking the mixture for a few minutes, and filtering it (except for the aqueous solution). The reported spectra of 5-methoxy-2-nitrosophenol in ethanol and water have been determined in the presence of a small amount of sulphuric acid (to inhibit dissociation), although the effect has been found to be negligible.

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Studies of Aspergillus niger. *Part IV.* The Synthesis of β-Linked Glucosaccharides.*

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A study has been made of the oligosaccharides formed from cellobiose by (*a*) growing cultures of *Aspergillus niger* (strain 152), (*b*) resting cells, and (*c*) cell-free extracts. It is shown that the enzyme system of the mould is able to transfer a glucose unit from cellobiose to another cellobiose molecule, to other β-linked disaccharides, or to glucose. The principal linkage synthesized is β-1 : 6, but β-1 : 2-, β-1 : 3-, and β-1 : 4-linkages are also formed. Indications have been obtained that D- and L-xylose, L-sorbose, and *N*-acetyl-D-glucosamine can also function as receptors in the transfer reaction.

As part of an investigation of the transglycosylation processes occurring in *Aspergillus niger* (strain 152, *i.e.*, the strain which synthesizes nigeran) (Barker, Bourne, and Stacey, *J.*, 1953, 3084), we have studied the metabolism of cellobiose by the mould. Just before publication of our preliminary results (Barker, Bourne, and Stacey, *Chem. and Ind.*, 1953, 1287), other workers reported that they had observed syntheses of oligosaccharides, of unknown constitution, during the action on cellobiose of enzymes obtained from *Aspergillus oryzae* (Jermyn and Thomas, *Austral. J. Biol. Sci.*, 1953, **6**, 70), *Aspergillus niger*, *Aspergillus aureus*, and *Myrothecium verrucaria*, and from the gut of the snail, *Helix pomatia* (Crook and Stone, *Biochem. J.*, 1953, **55**, xxv). More recently, Buston and Jabbar (*Chem. and Ind.*, 1954, **48**) and Giri, Nigam, and Srinivasan (*Nature*, 1954, **173**, 953) have made similar observations with cell-free extracts of *Chaetomium globosum* and *Aspergillus flavus*, respectively. We now describe the isolation and proof of structure of some of the complex mixture of oligosaccharides synthesized by *Aspergillus niger* (152), during growth on cellobiose, and also by the action on cellobiose of resting cells of the same organism.

The oligosaccharides produced in the culture filtrate of *Aspergillus niger*, which had been grown for 7 days at 30° on cellobiose (12·5% w/v) and the mineral constituents of Currie's medium, were fractionated on charcoal (Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677). Part of the small amount of glucose (1·3% of the initial weight of cellobiose) eluted from the column with water was isolated as crystalline α-D-glucose, the remainder being characterized as its β-penta-acetate. The 10%-ethanol eluate contained unchanged cellobiose, isolated as the crystalline sugar and as its β-octa-acetate, and traces of gentiobiose.

A complex series of six components having the mobilities of trisaccharides was detected in fractions obtained by elution with gradually increasing concentrations of ethanol (10—20%). Four of the trisaccharides I, III, V, and VI (numbered in their order of elution) were isolated almost chromatographically pure (>95%) but the others (II and IV) were only obtained as impurities in other fractions. Electrophoresis in the presence of borate buffer (pH 10) (Foster, *J.*, 1953, 982) enabled the saccharides to be classified into two distinct groups; one group (I, II) had M_G values similar to that of laminaritriose, while the others (III, IV, V, VI) had mobilities corresponding more closely to that of cellotriose. Since, under these conditions, a glucosaccharide in which the reducing unit is linked through $C_{(3)}$ or $C_{(6)}$ migrates much faster than an isomeric glucosaccharide with the reducing unit linked through $C_{(2)}$ or $C_{(4)}$ (cf. Foster, *loc. cit.*), and since the only disaccharide receptors detectable in the culture filtrate were gentiobiose and cellobiose, it seems likely that trisaccharides I and II had their reducing unit linked through $C_{(6)}$ and trisaccharides III, IV, V, and VI through $C_{(4)}$.

Complete hydrolysis of trisaccharides I, III, V, and VI gave only glucose. Partial hydrolysis of the same trisaccharides, and chromatographic and ionophoretic identification of the disaccharides produced, provided evidence sufficient to allow the tentative assignments of structure shown in Table 1.

Such assignments are in agreement also with the known order of elution from charcoal

* Part III, *J.*, 1954, 2125.

TABLE 1.

Trisaccharide	Partial hydrolysis products	Probable point of linkage * A	Probable point of linkage * B
I	Gentiobiose, glucose	β-1 : 6	β-1 : 6
II †	—	?	β-1 : 6
III	Gentiobiose, cellobiose, glucose	β-1 : 6	β-1 : 4
IV †	—	?	β-1 : 4
V	Cellobiose, glucose	β-1 : 4	β-1 : 4
VI	Cellobiose, laminaribiose, glucose	β-1 : 3	β-1 : 4

* A = non-reducing end; B = reducing end. † Disaccharide?

(gentiobiose, sophorose, cellobiose, and laminaribiose) of the β-linked glucose disaccharides. The infrared spectra of the trisaccharide mixture, and of the individual trisaccharides III, V, and VI, indicated that the linkages were predominantly of the β-type (cf. Barker, Bourne, Stacey, and Whiffen, *J.*, **1954**, 171), although this did not, of course, exclude the possibility that traces of α-linked saccharides were also present. The low specific rotations of trisaccharides I and III (approximately +4·1° and +10·2°, at equilibrium, respectively) were consistent with this conclusion; Lindberg and MacPherson (*Acta Chem. Scand.*, 1954, **8**, 985) reported $[\alpha]_D$ −6·5° for gentiotriose (I).

Trisaccharide III was produced in by far the largest amount (*ca.* 75% of the total trisaccharides) and so it was possible to obtain further confirmation of the structure already assigned to it. Partial hydrolysis of the aldonic acid produced by oxidation with hypoiodite gave a product with the same R_F value as gentiobiose, but no cellobiose. Trisaccharide III was reduced with sodium borohydride and the product was partially hydrolysed; specific spraying reagents showed that the products were gentiobiose, cellobiitol, glucose, and sorbitol. These observations indicated that III was indeed *O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl-(1→4)-D-glucopyranose. It follows that the corresponding glycitol should consume 7·0 mols. of periodate and give 3·0 mols. of formic acid and 2·0 mols. of formaldehyde and the observed figures (6·9, 2·9, and 1·8 mols., respectively) corresponded closely to these values. Of all the possible β-linked glucopyranose trisaccharides only one other [*O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl-(1→3)-D-glucopyranose] would have shown this behaviour during periodate oxidation of its alcohol.

Resting cells of *A. niger* incubated with cellobiose (10 g.; 20% w/v) for 7 days gave large amounts of glucose, and a series of disaccharides, whose R_F values were identical with those of gentiobiose, cellobiose, sophorose, and laminaribiose, as well as a complex mixture of trisaccharides. Fractionation on charcoal and elution with water and 5% ethanol led to the recovery of the glucose fraction (4·7 g.), most of which was obtained as the crystalline α-anomer.

Elution with 12·5% ethanol gave two fractions, one (0·6 g.) containing gentiobiose and a small amount of sophorose, and the other (0·7 g.) containing gentiobiose, cellobiose, and laminaribiose. Refractionation of the former on charcoal gave a fraction containing chromatographically-pure gentiobiose, which was characterized by conversion into its crystalline β-octa-acetate. The sophorose could be obtained in this way only in admixture with gentiobiose and so a portion of the mixture was separated on several ionophoretograms run in borate buffer (pH 10). Areas of paper containing sophorose were eluted under slightly acid conditions and the ions present were removed by using an ion-exchange column, electrodialysis, and co-distillation with methanol; the sophorose was isolated as a freeze-dried powder. When treated with phenylhydrazine it gave glucosazone; this reaction is shown only by disaccharides in which the sugar units are linked 1 : 2 and is typical in general of 2-substituted aldoses (*e.g.*, 2-*O*-methyl-D-glucose).

In order to facilitate the identification of laminaribiose, advantage was taken of the observation that the action of resting cells on cellobiose produced mainly laminaribiose during the initial stages and gentiobiose in the later stages. Accordingly, a cell-free extract of *A. niger* was incubated with cellobiose for three days and a crude cellobiose–laminaribiose fraction was isolated by using a charcoal column. The basis of the subsequent separation was that laminaribiose forms a furanoside mixture when treated with methanolic hydrogen chloride at room temperature (which cellobiose cannot do) and the glucosidic substituent exerts a retarding influence when the substance is passing through charcoal (cf. Barker, Bourne, and O'Mant, *Chem. and Ind.*, 1955, 425). In this way, methyl

αβ-laminaribiofuranoside was obtained free from cellobiose and freeze-dried. Oxidation with periodate confirmed the structure. All the disaccharides were hydrolysed readily by an almond emulsin preparation, which had negligible action on the α-linked disaccharides maltose and nigerose.

It is interesting that disaccharide formation by the resting cells shows such a marked contrast with the results obtained with growing cultures, which gave a trace of gentiobiose only. The reason seems to be that the cultures metabolize much of the glucose formed in the transfer reaction, so that it is not available as a receptor in disaccharide synthesis.

The complex mixture of at least nine trisaccharides synthesized by the resting cells from cellobiose was examined only by paper chromatography and paper ionophoresis. Most of the trisaccharides (I—VI) synthesized by the growing cells could be detected. The remainder presumably arose through the ability of laminaribiose, sophorose, and the increased quantity of gentiobiose to function as receptors of transferred glucose units. Confirmatory evidence that this was so was obtained when trisaccharides were detected following the incubation of enzyme extracts with gentiobiose and with laminaribiose.

Thus it is clear that the enzyme system of the 152 strain of *Aspergillus niger* catalyses the transfer of glucose from cellobiose to glucose, to cellobiose itself, and to other β-linked glucose disaccharides, with the formation of β-1 : 2-, β-1 : 3-, β-1 : 4-, and β-1 : 6-linkages, of which the last predominates; if α-linkages are produced then they constitute a very small proportion of the total. It is not essential for the receptor to be glucose or its higher homologues, because evidence has been obtained that D- and L-xylose, L-sorbose, and *N*-acetyl-D-glucosamine can function in the same way; structural examinations of the products are now in progress. The fact that D-xylose can serve as a receptor is interesting in view of its common natural occurrence in association with D-glucose, and the close stereochemical relationship between the two sugars. It is significant also that its optical enantiomorph, and also L-sorbose which differs only at the reducing position from L-xylose, should be receptors. These observations raise interesting problems regarding enzyme specificity, but it would be unwise to speculate further at this stage, since it remains to be proved whether all the reactions observed are due to the same enzyme or to several.

During the preparation of this manuscript, Peat, Whelan, and Hinson (*Chem. and Ind.*, 1955, 385) published a preliminary account of studies with an enzyme extract of *Aspergillus niger* NRRL 330 in which they demonstrated the formation from glucose of ten disaccharides, which belonged to both the α- and β-series. In addition, Pfanmüller and Noë (*Science*, **1952**, **115**, 240) and Aso and Shibasaki (*Tohoku J. Agric. Res.*, **1953**, **3**, 337) have found that *A. oryzae* and *A. niger* concentrates give *iso*maltose from glucose. These reports prompt the question whether the syntheses which we have observed from cellobiose were direct transfer reactions, or whether they entailed hydrolysis to glucose and subsequent resynthesis. We believe that the former alternative is the correct one in this case because, in contrast to the latter, it explains the formation of disaccharides by the resting cells, but not by the growing cultures, and also the fact that the main trisaccharide is *O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl-(1→4)-D-glucopyranose. Moreover, cell-free extracts of *A. niger* (strain 152) synthesize principally *iso*maltose and panose from maltose (Barker and Carrington, *J.*, **1953**, **3588**), so that, with at least one of the two disaccharide substrates, hydrolysis is not an essential step in the synthesis of glucosaccharides. It will be recalled that Peat, Whelan, and Hinson (*Nature*, **1952**, **170**, 1056) demonstrated that almond emulsin produces β-linked oligosaccharides from high concentrations of glucose; we have now shown that cellobiose is an alternative substrate, but it remains to be proved whether a direct transfer is involved. An interesting problem which is beginning to emerge is whether the synthesis of α- and β-oligosaccharides by moulds necessarily results from two different enzymes, or whether the anomeric character of the products is determined solely by that of the substrate (maltose, α-glucose; cellobiose, β-glucose).

Experimental

Production of Glucosaccharides by Growing Cells.—A sterile solution (160 c.c.), containing cellobiose (20 g.) and the mineral components of Currie's medium (*J. Biol. Chem.*, **1917**, **31**, 15), was inoculated with *Aspergillus niger* " **152** " and incubated at 30°. Spots of the solution were

removed at intervals and analysed chromatographically as the free sugars and as their benzylamine derivatives (Bayly and Bourne, *Nature*, 1953, **171**, 385) with *n*-butanol (40%)–ethanol (10%)–water (49%)–ammonia (1%) as solvent. The disappearance of cellobiose and the gradual production of components having the mobilities of trisaccharides, together with traces of glucose and gentiobiose, were detectable after spraying with aniline hydrogen phthalate (Partridge, *Nature*, 1949, **164**, 443). After 7 days, the culture filtrate and mycelial washings were adjusted to pH 7 with sodium hydroxide and boiled for 20 min. to arrest enzyme action. The cooled solution was passed through charcoal (30 × 3·4 cm. diam.) and the glucosaccharides fractionated by elution with increasing concentrations of aqueous ethanol (Whistler and Durso, *loc. cit.*). After analysis by paper chromatography and by paper ionophoresis in borate buffer, pH 10 (Foster, *loc. cit.*), similar fractions were combined, concentrated, purified by methanol extraction, and obtained as syrups or freeze-dried powders.

Characterization of the Oligosaccharide Fractions.—Elution with water (1050 c.c.) gave a fraction (0·25 g.) which contained a single sugar component with an R_P value equal to that of glucose. Crystallization from methanol gave α-D-glucose (0·15 g.), m. p. and mixed m. p. 146°, $[\alpha]_D^{18}$ +52·0° (equil.; *c*, 0·56 in H_2O) (Found: C, 40·4; H, 6·9. Calc. for $C_6H_{12}O_6$: C, 40·0; H, 6·7%). The residual glucose was isolated as its β-penta-acetate (0·14 g.), m. p. and mixed m. p. 131°, $[\alpha]_D^{18}$ +3·7° (*c*, 0·43 in $CHCl_3$) (Found: C, 49·1; H, 5·6. Calc. for $C_{16}H_{22}O_{11}$: C, 49·2; H, 5·7%).

Elution with 10% ethanol (2 l.) gave fractions containing cellobiose and traces of gentiobiose. Crystallization from methanol afforded β-cellobiose (1·68 g.), m. p. and mixed m. p. 224—225°, $[\alpha]_D^{19}$ +35·1° (equil.; *c*, 0·84 in H_2O) (Found: C, 42·6; H, 6·9. Calc. for $C_{12}H_{22}O_{11}$: C, 42·1; H, 6·5%). Cellobiose (0·050 g.) was further characterized as its β-octa-acetate (0·072 g.), m. p. and mixed m. p. 200°, $[\alpha]_D^{18}$ −15·7° (*c*, 0·26 in $CHCl_3$) (Found: C, 49·35; H, 5·55. Calc. for $C_{28}H_{38}O_{19}$: C, 49·6; H, 5·6%).

Gradient elution with 10—20% ethanol (3100 c.c.) gave a series of fractions (total wt., 1·432 g.) which contained trisaccharides only. By paper ionophoresis and paper chromatography jointly, six different trisaccharides were distinguished; they were numbered I—VI in order of elution from the column. Their behaviour on chromatograms (as the free sugars) and on ionophoretograms (methods as above) is shown in the following Table.

Trisaccharide	$R_{\text{cellotriose}}$	$R_{\text{laminaritriose}}$	M_G *value approx. same as that of:*
I	0·8	0·4	Laminaritriose
II	2·3	1·1	Laminaritriose
III	1·3	0·6	Cellotriose
IV	3·0	1·4	Cellotriose
V	1·0	0·45	Cellotriose
VI	1·8	0·8	Cellotriose

Traces (5—15 mg.) only of II and IV were obtained as impurities in other fractions and these were not investigated further. Trisaccharide III was present in largest amount (*ca.* 1·1 g.), followed by trisaccharide I (190 mg.) and small quantities of trisaccharides V and VI (30—50 mg.).

Samples of trisaccharides I, III, V, and VI (5 mg. of each) were hydrolysed with N-sulphuric acid (1 c.c.) at 100° for 5 hr. Each hydrolysate was almost neutralized with barium carbonate and filtered, and the residual ions removed by electrodialysis (Consden, Gordon, and Martin, *Biochem. J.*, 1947, **41**, 590). Analysis by paper ionophoresis and paper chromatography, as previously described, revealed only one component, having R_P and M_G values identical with those of glucose, in each hydrolysate.

Partial hydrolysis of samples (5 mg.) of trisaccharides I, III, V, and VI was effected by heating them in N-sulphuric acid (0·5 c.c.) at 100° for 20 min. Removal of ions and analysis by the above methods indicated that trisaccharide I gave gentiobiose and glucose, trisaccharide III gave gentiobiose, cellobiose, and glucose, trisaccharide V gave cellobiose and glucose, and trisaccharide VI gave laminaribiose, cellobiose, and glucose.

Infrared analysis of trisaccharides III, V, and VI (as mulls in liquid paraffin) showed marked absorption at 896 cm.$^{-1}$, but little at 840 cm.$^{-1}$, indicating the presence of β-links in the three trisaccharides (Barker, Bourne, Stacey, and Whiffen, *loc. cit.*).

Further Examination of Trisaccharide III.—(a) *Partial hydrolysis of the aldonic acid of trisaccharide III.* The trisaccharide (10 mg.) was oxidized with a solution (8 c.c.) containing 0·1N-iodine (1 c.c.) and 0·2M-bicarbonate buffer (2 c.c.; pH 10·6). After 3 hr. at room temperature, the excess of iodine was destroyed with sodium thiosulphate, and the aldonic acid was partially hydrolysed by addition of N-sulphuric acid (1 c.c.) and heating the solution at 100°

for 25 min. Paper-chromatographic analysis revealed a component having the same mobility as gentiobiose; no cellobiose was detected.

(b) *Partial hydrolysis of the alcohol from trisaccharide III.* An aqueous solution (12 c.c.) of the trisaccharide (100 mg.) and sodium borohydride (50 mg.) was kept at room temperature until the optical rotation was constant (*ca.* 2 hr.). After destruction of the excess of borohydride with acetic acid, N-sulphuric acid (5 c.c.) was added. The solution was heated at 100° for 20 min. and then neutralized, filtered, and de-ionized in the usual manner.

Portions of the hydrolysate were separated on duplicate chromatograms run in the organic phase of the butanol solvent mixture previously described. One of these, having glucose, cellobiose, and gentiobiose as references, was sprayed with aniline hydrogen phthalate and showed the presence of components with the mobilities of gentiobiose and glucose. The other chromatogram, having cellobiitol and sorbitol as references, was sprayed with a solution of bromocresol purple (40 mg.) in 95% methyl alcohol (100 c.c.) containing boric acid (100 mg.) to which 1% borax solution (7·5 c.c.) had been added (Bradfield and Flood, *Nature*, 1950, **166**, 264). This showed the presence of components having the mobilities of cellobiitol and sorbitol.

(c) *Periodate oxidation of the alcohol from trisaccharide III.* A sample of trisaccharide III (50 mg.) was reduced with sodium borohydride then treated with acetic acid and electrodialysed, as described previously. The boric acid was removed by three distillations with methanol, and the residual sugar alcohol was dissolved in water and freeze-dried. Chromatographic analysis, and use of the bromocresol-purple spray (see above), showed one spot due to the trisaccharide alcohol, but no cellobiitol or sorbitol.

An aqueous solution (10 c.c.) of the alcohol of trisaccharide III (42 mg.) was added to 0·25M-sodium periodate (15 c.c.), diluted to 50 c.c., and kept at 17°. Aliquot portions (5 c.c.) of the solution were withdrawn at intervals and neutralized with solid sodium hydrogen carbonate, and the periodate determined by addition of excess of standard sodium arsenite solution and back-titration of the excess of arsenite with standard iodine solution (Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107, 196). The periodate content at zero time was determined in a suitable blank from which the carbohydrate had been omitted. The periodate consumption, expressed in moles per mole of alcohol was : 6·8 (2 hr.), 6·9 (20 hr.).

After 20 hr., a portion (5 c.c.) was treated with ethylene glycol and titrated against 0·02N-sodium hydroxide, methyl red being used as indicator; the result indicated that the formic acid production was 2·9 moles per mole of alcohol.

After 20 hr., the formaldehyde present in 5 c.c. of the solution was determined by addition of an excess of dimedone (10%) in alcohol. After filtration and drying at 110° to constant weight, the amount of dimedone derivative corresponded to 1·8 moles of formaldehyde per mole of alcohol taken.

Production of Glucosaccharides by Resting Cells.—An aqueous solution (50 c.c.) of cellobiose (10 g.) was incubated for 7 days with freeze-dried *Aspergillus niger* cells (1 g.) at 30°. Paper-chromatographic analysis showed the disappearance of cellobiose and the gradual production of glucose and trisaccharides, together with three disaccharides having the mobilities of gentiobiose, sophorose, and laminaribiose. In the initial stages, laminaribiose was the main disaccharide produced, but in the later stages of incubation by far the greatest proportion of the disaccharide fraction was gentiobiose. After 7 days the digest filtrate was adjusted to pH 7 with sodium hydroxide and enzyme action arrested by heating the solution at 100° for 20 min. The saccharide mixture was fractionated on charcoal (30 × 3·4 cm. diam.) by Whistler and Durso's method (*loc. cit.*) and fractions (200 c.c.) analysed and obtained as syrups or freeze-dried powders in the manner previously described.

Further Purification and Characterization of Oligosaccharide Fractions.—Elution with water (1600 c.c.) and 5% ethanol (600 c.c.) gave a fraction (4·691 g.) which contained glucose and a trace of gentiobiose. When crystallized from methanol, α-D-glucose (3·537 g.) was obtained, m. p. and mixed m. p. 140—142°.

Elution with 10% ethanol (800 c.c.) and 12·5% ethanol (800 c.c.) gave fraction *A* (0·630 g.) which contained gentiobiose, together with a small amount of sophorose. Further elution with 12·5% ethanol (2000 c.c.) gave a mixture (0·692 g.) of gentiobiose, cellobiose, and laminaribiose. Refractionation of *A* on charcoal gave one fraction containing pure gentiobiose and another containing a mixture of gentiobiose and sophorose. A portion (0·065 g.) of the chromatographically pure gentiobiose was acetylated at room temperature with acetic anhydride (1·5 c.c.) and pyridine (1·5 c.c.). Isolated in the usual way and crystallized from methanol, the β-gentiobiose octa-acetate (0·032 g.) had m. p. and mixed m. p. 193°, $[\alpha]_D^{17}$ −5·0° (*c*, 0·14 in $CHCl_3$) (Found : C, 50·0; H, 5·7. Calc. for $C_{28}H_{38}O_{19}$: C, 49·6; H, 5·6%).

A portion (20 mg.) of the gentiobiose–sophorose mixture, in water, was streaked across a Whatman No. 3 filter paper (57 × 13 cm.) and separated by ionophoresis in borate buffer (pH 10) at 500 volts for 6 hr. and the ionophoretogram left to dry in air. Marker strips (1 cm.) were cut off six such papers and sprayed with aniline hydrogen phthalate to indicate the positions of the two components. The total area (472·5 cm.²) of paper containing sophorose was eluted with 0·01N-hydrochloric acid (232 c.c.). The filtrate and washings of the paper pulp were passed down a column of Amberlite 120H directly on to silver carbonate. This procedure removed sodium, chloride, and most of the borate ions. The filtrate was concentrated to 5 c.c. and the residual silver and chloride ions removed by electrodialysis. The solution was then concentrated to a syrup and co-distilled three times with methanol *in vacuo* to remove all borate. After the residue had been dissolved in water the sophorose was freeze-dried (13 mg.); it was ionophoretically pure.

Part (2 mg.) of the sophorose was hydrolysed with N-sulphuric acid (1 c.c.) at 100° for 1 hr.; only one component, having an R_F value equal to that of glucose, could be detected in the hydrolysate. An aqueous solution (1 c.c.) of the remaining sophorose (10 mg.) was heated with a solution of freshly distilled phenylhydrazine (0·2 c.c.) in acetic acid (0·4 c.c. of acid in 1 c.c. of water) for 1·5 hr. at 100°. The recrystallized product (12 mg.) had m. p. 207° alone and in admixture with glucosazone (Found: C, 59·9; H, 6·25; N, 15·2. Calc. for $C_{18}H_{22}O_4N_4$: C, 60·3; H, 6·2; N, 15·6%).

Elution with 12·5—27·5% alcohol (5200 c.c.) gave a series of fractions (total yield, 0·967 g.) in which at least nine suspected trisaccharides could be detected by combining the evidence supplied by paper ionophoresis in borate buffer (pH 10) and paper chromatography in the butanol solvent mixture previously described.

Isolation of Laminaribiose.—Cellobiose (2 g.) and a cell-free extract of *Aspergillus niger* " 152 " were incubated at 30° for three days; the main disaccharide produced was then laminaribiose. Fractionation on charcoal (17 × 3·4 cm. diam.) gave a fraction (1·01 g.) containing only cellobiose and laminaribiose. This was treated with 4% methanolic hydrogen chloride (35 c.c.) at room temperature for 2 hr. After addition of excess of silver carbonate the pH rose to *ca.* 5. The suspension was filtered and the methanol removed *in vacuo* in the presence of a little freshly-washed barium carbonate. The syrupy residue was suspended in water, filtered, and passed through acid-free charcoal. Washing with increasing concentrations of aqueous ethanol removed the cellobiose first and later gave fractions which were non-reducing but contained a component which had an M_G value slightly greater than that of cellobiose when separated as its borate complex on a ionophoretogram. This component, presumably the mixed methyl furanoside of laminaribiose, could be detected with an alkaline silver nitrate spray (Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444).

A portion (79 mg.) of the freeze-dried glycoside was oxidized with periodate by the method previously described. After 20 hr., the periodate consumption was 3·3 moles per mole of furanoside; and the amounts of formic acid and formaldehyde produced were 0·8 and 1·3 moles per mole, respectively. The theoretical figures for a methyl furanoside of laminaribiose are 3·0, 1·0, and 1·0, respectively.

The Action of Almond Emulsin on Cellobiose.—Emulsin (10 mg.), prepared from bitter almonds by a method similar to that of Bourquelot and Bridel (*Ann. Chim. Phys.*, 1913, **29**, 145), was added to an aqueous solution (1 c.c.) of cellobiose (20% w/v) and aliquot portions submitted to paper-chromatographic analysis at intervals. Components were produced during the incubation which had R_F values identical with those of glucose, gentiobiose, laminaribiose, and higher saccharides.

Investigation of Possible Receptors in β-Transglucosylation.—A suspension of freeze-dried cells of *A. niger* (1·5 g.) in water (8 c.c.) was shaken with glass beads for several hours in a Mickle Tissue Disintegrator and the cell debris removed by centrifugation. Equal weights (150 mg.) of cellobiose and the possible receptor (D- and L-xylose, D-ribose, L-sorbose, L-arabinose, and *N*-acetyl-D-glucosamine) were dissolved severally in portions (1 c.c.) of the cell-free enzyme extract and chromatographic analyses carried out on each solution at frequent intervals during the first day and thereafter at daily intervals. All chromatograms were sprayed with aniline hydrogen phthalate and in the case of L-sorbose a duplicate was sprayed with naphtharesorcinol. In the cases of the cellobiose–D-xylose and cellobiose–L-xylose mixtures components, presumably two glucose-xylose disaccharides, were detected additional to those produced on incubation of the cell-free extracts and cellobiose alone. These additional components had R_F values intermediate between those of cellobiose and glucose when separated in the butanol solvent mixture and gave a pink colour with aniline hydrogen phthalate. There was evidence

also that L-sorbose and *N*-acetyl-D-glucosamine functioned as receptors in the formation of oligosaccharides.

The authors thank the Nuffield Foundation and the British Rayon Research Association for financial assistance. One of them (G. C. H.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant.

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EDGBASTON, BIRMINGHAM, 15. [*Received, May 20th*, 1955.]

A New Optically Active Flavanone from the Leaves of Rhododendron farrerae, *Tate.*

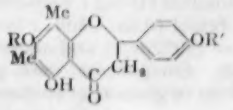
By H. R. ARTHUR.

[Reprint Order No. 6467.]

A new optically active flavanone, for which the name farrerol is proposed, has been isolated from the leaves of *Rhododendron farrerae*. It has been shown to be 5 : 7 : 4′-trihydroxy-6 : 8-dimethylflavanone (4′-demethylmatteucinol) and so it has, in common with two of the other known optically active naturally occurring flavanones, methyl groups in the 6- and 8-positions.

ARTHUR and HUI (*J.*, 1954, 4683) reported that the leaves of the *Rhododendrons* of Hong Kong contain the triterpene acid, ursolic acid; they also showed (*ibid.*, p. 2782) that the leaves of *R. simsii* contain in addition the flavanone, matteucinol. Examination of the leaves of the other *Rhododendrons* of Hong Kong in the manner adopted for *R. simsii* (*loc cit.*) reveals the presence of a new flavanone (hereafter called "farrerol") in *R. farrerae*, but flavonoid compounds were not obtained from *R. championae*, *R. westlandii*, or *R. simiarum*. It is noteworthy that the two *Rhododendrons* which yield flavanones are alone in that they possess small leaves, and further, that their leaves possess a soft brown pubescence. The behaviour of farrerol indicated that it occurs in the plant in an optically active form and that it partly racemised during extraction and purification. From (±)-farrerol triacetate, (±)-farrerol was prepared and characterised as the dimethyl ether, the oxime, and the corresponding chalkone.

Since optically active flavanones which have previously been isolated include matteucinol and demethoxymatteucinol [Fujise, *Sci. Papers Inst. Phys. Chem. Res.* (*Tokyo*), 1929, **11**, 111] and since Arthur and Hui (*J.*, 1954, 2782) showed that matteucinol is present in the leaves of *Rhododendron simsii*, it was considered that farrerol (I) may have been related to matteucinol (II). This relationship was established when (±)-farrerol yielded



(I; R = R′ = H)
(II; R = H, R′ = Me)
(III; R = R′ = Me)

(±)-matteucinol monomethyl ether (III) on methylation with diazomethane. (±)-Farrerol was shown, finally, to be 5 : 7 : 4′-trihydroxy-6 : 8-dimethylflavanone, since it is identical with the demethylation product of (±)-matteucinol.

Attempts to resolve (±)-farrerol by the use of (−)-menthoxyacetyl chloride failed. An attempt was also made to obtain (−)-farrerol from the plant by a method which avoided the use of alkali. This gave a product richer in (−)-farrerol than that which had previously been obtained, but still not optically pure.

The structural regularity (methyl groups at the 6- and the 8-position) of farrerol and the two naturally occurring optically active flavanones matteucinol and demethoxymatteucinol is noted. Hillis (*Austral. J. Sci. Res.*, 1952, *A*, **5**, 379) reports that 3 : 5 : 7 : 4′-tetrahydroxyflavanone (dihydrokaempferol) obtained from the kinos of *Eucalyptus calophylla* and *E. corymbosa* is optically active.

Experimental

M. p.s are corrected. Analyses are by Dr. Zimmermann, Melbourne. Rotations are in acetone.

Isolation of the Flavanone.—Leaves (4 kg.) were extracted with ether (10 l.) and the ethereal extract was worked up as stated for that of *Rhododendron simsii* (*J.*, 1954, 2783). The crude yellow flavanone (34 g., 0·85%) was recrystallised from aqueous dioxan. Buff-coloured fern-like crystals (20 g., 0·5%) of a mixture of (−)-farrerol and (±)-farrerol separated. This mixture which gave the usual colour reactions for flavanones had m. p. 207—218°, $[\alpha]_D$ −16°, and further recrystallisations from aqueous dioxan or from other solvents did not improve the m. p.

(±)-*Farrerol Triacetate.*—Acetylation by acetic anhydride and sodium acetate gave a complex mixture which contained the chalkone acetate. The flavanone was therefore acetylated by Bannerjee and Seshadri's method (*Proc. Indian Acad. Sci.*, 1952, **36**, *A*, 138). To an ice-cooled solution of the farrerol mixture ($[\alpha]_D$ −16°) (2·5 g.) in pyridine (10 ml.), acetyl chloride (6·0 ml.) was added dropwise during 1 hr. Next morning the product ($[\alpha]_D$ +10°) (2·2 g.), isolated as usual, was recrystallised 7 times from methanol, then once from ethanol. The (±)-*triacetate* (1·1 g.), which separated in rectangular plates, m. p. 192°, $[\alpha]_D$ 0·02° (*c*, 0·81) (Found: C, 64·5; H, 5·2; Ac, 30·1%; *M*, 378. $C_{23}H_{22}O_8$ requires C, 64·8; H, 5·2; 3Ac, 30·3%; *M*, 426), was unchanged after chromatography (acetone solution over alumina). It gave no colour with ferric chloride solution and a magenta colour with hydrochloric acid and magnesium in methanol; it was insoluble in dilute sodium hydroxide solution.

(±)-*Farrerol.*—(a) *By deacetylation of* (±)-*farrerol triacetate.* The triacetate (0·5 g.) was deacetylated with dilute ethanolic sulphuric acid (40 ml.). The crude product which was recrystallised from aqueous dioxan separated as buff-coloured needles of (±)-*farrerol*, m. p. 223—224° (Found: C, 67·9; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%). This compound was very soluble in methanol, soluble in dioxan, and sparingly soluble in water and light petroleum. It gave a green colour with ferric chloride solution in ethanol, a bright red colour with magnesium and hydrochloric acid in methanol, and an intense vermillion-red solution with aqueous sodium hydroxide.

(b) *By fractional recrystallisation of the farrerol mixture from the plant.* The mixture, m. p. 206—218° (10 g.), was dissolved in methanol (25 ml.). The first crop (0·5 g.) obtained as solvent evaporated had m. p. 223° and $[\alpha]_D$ −1·1°, and on recrystallisation yielded almost inactive farrerol, m. p. 223—224° [not depressed by the product from (a)], $[\alpha]_D$ −0·8°.

(c) *By racemisation of the farrerol mixture.* The mixture, m. p. 206—218° (0·5 g.), was dissolved in 0·2N-aqueous alcoholic potassium hydroxide solution (30 ml.) and the solution was left for 2 days. The precipitate was removed, and then the filtrate on acidification yielded (±)-farrerol, m. p. 223° after one recrystallisation from dioxan.

(d) *By demethylation of* (−)*-matteucinol.* (i) (−)-Matteucinol (2·0 g.) was demethylated in a mixture of acetic anhydride (10 ml.) and 55% hydriodic acid (10 ml.). The product, on recrystallisation from aqueous ethanol, yielded almost colourless needles (1·1 g.) of (±)-farrerol, m. p. 223° alone or on admixture with the product from (a). Longer heating or increased temperature produced quantities of a bright red compound.

(ii) (−)-Matteucinol (1·0 g.) was demethylated with dry benzene and freshly powdered anhydrous aluminium chloride (6 g.). The product, isolated in the usual manner, on recrystallisation from aqueous methanol gave (±)-farrerol, m. p. 223°. An intensely red and fluorescent by-product, which was not further investigated, was also obtained.

These samples of (±)-farrerol [from d(i) and d(ii)] were further identified by conversion into 2′ : 4′ : 6′ : 4-tetra-acetoxy-3′ : 5′-dimethylchalkone (see below).

(±)-*Farrerol* 7 : 4′-*Dimethyl Ether.*—This was prepared from (±)-farrerol with diazomethane in ether. Recrystallisation from methanol gave pale yellow needles, m. p. 102° alone or in admixture with (±)-matteucinol monomethyl ether (Found: C, 69·1; H, 6·3; OMe, 18·7. Calc. for $C_{19}H_{20}O_5$: C, 69·5; H, 6·1; 2OMe, 18·9%).

(±)-*Farrerol Oxime.*—(±)-Farrerol (0·4 g.) was heated in aqueous ethanol with sodium acetate (0·5 g.) and hydroxylamine hydrochloride (0·5 g.) for 17·5 hr. The product on recrystallisation from aqueous methanol yielded colourless needles, m. p. 253—255°, of the *oxime* (Found: C, 65·4; H, 5·6; N, 4·3. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4; N, 4·4%), which became bright yellow on exposure to air and light; it gave a magenta-coloured solution with magnesium and hydrochloric acid in methanol.

2′ : 4′ : 6′ : 4-*Tetra-acetoxy-3′* : 5′-*dimethylchalkone.*—A solution of (±)-farrerol triacetate (0·5 g.) in acetic anhydride (15 ml.) was boiled under reflux for 9 hr., and then poured into water.

The product which separated was recrystallised 4 times from methanol. The *chalkone* was obtained as colourless needles, m. p. 158—159° (Found : C, 64·2; H, 5·2; Ac, 35·7. $C_{23}H_{24}O_9$ requires C, 64·1; H, 5·1; 2 Ac, 36·7%).

Attempted Isolation of (−)-Farrerol.—Leaves (2 kg.) were extracted with cold light petroleum (b. p. 60—80°; 10 l.), then with ether (10 l.). The ethereal extract was evaporated to dryness and the greenish-black residue which remained was extracted with quantities of warm methanol until the extract showed a negative reaction for flavonoid compounds with magnesium and hydrochloric acid. The combined methanol extracts were treated with charcoal and then concentrated in stages (crops of triterpenoid material being removed after each concentration) until the extract failed to deposit triterpenoid material. The methanol extract was then evaporated almost to dryness. The greenish-black crop of crude flavanone was collected from the black filtrate. The crude flavanone was recrystallised several times from dioxan and aqueous dioxan (charcoal). Cream-coloured needles (0·2%) of a mixture of (−)-farrerol and (±)-farrerol, m. p. 213—217°, $[\alpha]_D$ −18·7° (*c*, 0·66) were obtained (Found : C, 68·4; H, 5·5. Calc. for $C_{17}H_{16}O_5$: C, 68·0; H, 5·3%). Acetylation of this material yielded an optically active acetate, m. p. 176—179° (after 8 recrystallisations from methanol), mixed m. p. with (±)-farrerol triacetate, 188—190° after contraction at 180°. This was considered to be very rich in (+)-farrerol triacetate, but, from the way in which it separated from organic solvents and from its m. p. range, was not considered to be pure.

The author thanks Professor J. E. Driver for his interest, Mr. H. C. Tang (Government Herbarium, Hong Kong) for identification of plant material, and Mr. C. W. Pan for assistance in its collection.

UNIVERSITY OF HONG KONG, HONG KONG. [*Received, June 1st,* 1955.]

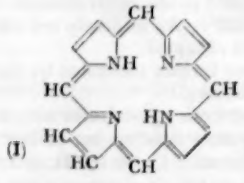
Chlorophyll and Related Substances. Part I. The Synthesis of Chlorin.

By ULLI EISNER and R. P. LINSTEAD.

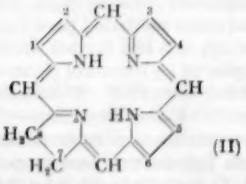
[Reprint Order No. 6389.]

Chlorin (II), the parent substance of chlorophyll, has been synthesised in one step from 2-dimethylaminomethylpyrrole (VI) in yields of up to 3·9%. Metal derivatives have been prepared. Light absorption data are given.

THE porphyrins, the most important colouring matters in Nature, can be divided into two main structural groups. These are, broadly, the "red" and the "green" pigments typified by hæmin and chlorophyll, respectively. The respective parent compounds of the two series are porphin (I) and chlorin (II), about which, respectively, little and nothing has hitherto been known.



(I)



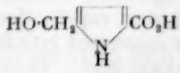
(II)

These conventional formulæ represent single possible canonical forms of resonance hybrids. There is no decisive evidence for the placing of the two "extra hydrogens" of chlorin on $C_{(7)}$ and $C_{(8)}$. This has been done in formula (II) following Hans Fischer's practice in analogous compounds. The general question of the place of the extra hydrogens will be the subject of a later communication.

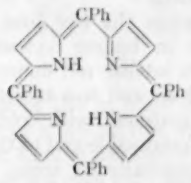
Two syntheses of porphin have been reported (Fischer and Gleim, *Annalen*, 1936, **521**, 157; Rothemund, *J. Amer. Chem. Soc.*, 1936, **58**, 625) but the amounts of material obtained were so small that its properties were not described in detail. Moreover, certain anomalies exist which have not been satisfactorily explained. Chlorin has never been prepared.

We now describe a synthesis of chlorin and its quantitative conversion into porphin, which is most readily prepared by the new method.

The methods described in the literature for the synthesis of porphyrins (Fischer and Orth, " Die Chemie des Pyrrols," Leipzig, 1937, Vol. II, p. 1) have in general been developed for compounds containing substituents on the β-carbon atoms of the pyrrolic intermediates. When these are unsubstituted, the methods fail either completely or almost so. Thus Siedel's method (*Annalen*, **1943**, **554**, 162) breaks down and no porphin was obtained from the intermediate (III). Fischer and Gleim's synthesis of porphin consisted in treating



(III)

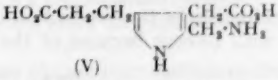


(IV)

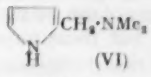
pyrrole-2-aldehyde with boiling formic acid, whilst Rothemund heated pyrrole with methanolic formaldehyde. The reported yields were of the order of 0·1%. The preparation of *ms*-tetraphenylporphin (IV) by the reaction between pyrrole and benzaldehyde (Rothemund, *J. Amer. Chem. Soc.*, 1941, **63**, 267; Priesthoff and Banks, *ibid.*, 1954, **76**, 937, *et seq.*) is, however, more favourable. Yields of up to 18% of the zinc derivative of (IV) have been reported and we have found no difficulty in preparing the compound by this method. The phenyl group appears to exercise its beneficial effect by inhibiting side-reactions involving an attack on the β-carbon atoms.

Excluding the *meso*-substituted compounds, all known chlorins carry β-groups. They have been prepared either by mild degradation of chlorophyll derivatives (Fischer and Orth, *op. cit.*, p. 2) or by the reduction of porphyrins. The only direct synthesis has been the formation of *ms*-tetraphenylchlorin as a by-product in the preparation of the corresponding porphin (IV) from pyrrole and benzaldehyde (Aronoff and Calvin, *J. Org. Chem.*, 1943, **8**, 205; *J. Amer. Chem. Soc.*, **1943**, **65**, 2259).

The compounds which we have examined as intermediates for the synthesis of porphins and chlorins are the Mannich bases (such as VI) derived from pyrrole. They have not previously been used for this purpose, but possess certain attractive features. The α-methylene group can provide the methine link, and it is known that Mannich bases condense with compounds containing an active methylene with loss of primary or secondary amine. A particular instance is self-condensation, for example the formation of di-(1-methyl-2-indolyl)methane from *N*-methylgramine (Snyder and Eliel, *J. Amer. Chem. Soc.*, 1949, **71**, 663). Moreover, the recent work of Cookson and Rimington (*Nature*, 1953, **171**, 875; **172**, 292, 457; *Biochem. J.*, 1954, **57**, 476) provided favourable indications. They showed that the naturally occurring porphyrin precursor porphobilinogen (V), which is a substituted Mannich base, was converted into uroporphyrin under mild conditions.



(V)



(VI)

We accordingly prepared 2-dimethylaminomethylpyrrole (VI) following Herz, Dittmer, and Cristol * (*J. Amer. Chem. Soc.*, 1947, **69**, 1698). Preliminary experiments were carried out on the action of the following agents on the base (VI) or its methiodide: heat, boiling formic acid, dilute hydrochloric acid (cf. Cookson and Rimington, *loc. cit.*), sodamide, magnesium formate, zinc acetate, ferric or mercurous chlorides, sodium or magnesium hexyloxides (cf. Linstead and Whalley, *J.*, 1952, 4839). All failed to give a porphyrin-type pigment. Heating the base (VI) with cuprous chloride in boiling decalin, xylene, or toluene gave copper porphin in very low yield. This was purified by chromatography; the spectrum agreed well with that recorded by Stern (*Z. phys. Chem.*, 1936, **177**, *A*, 58) for

* The method gave erratic results with the occasional formation of much polymeric material.

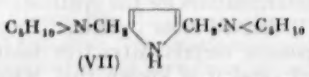
Fischer's material. Treatment of the base (VI) with a mixture of stannic and stannous chlorides in boiling xylene gave a purplish-blue pigment, with a porphyrin-type of light absorption, which was not obtained homogeneous.

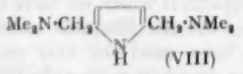
As, however, our primary objective was the metal-free pigment, we concentrated on procedures involving a labile metal. Snyder, Eliel, and Carnahan (*J. Amer. Chem. Soc.*, 1951, **73**, 970) have investigated the reaction between the methiodide of (VI) and methylmagnesium iodide in boiling *n*-butyl ether with the object of determining whether alkylation of the pyrrole nucleus occurred. They detected no alkylation, nor did they record the formation of pigment.

We found that when the free base (VI) was heated with one equivalent of ethylmagnesium bromide in boiling xylene it yielded magnesium chlorin as a greenish blue solution with an intense red fluorescence. The pigment rapidly decomposed in the presence of light and air and was therefore immediately converted into the stable metal-free compound by treatment with cold dilute hydrochloric acid. The overall yields of chlorin were fairly reproducible and of the order of 1%. (This and subsequent yields were determined spectroscopically by using data subsequently determined for pure chlorin.) The method of isolating the chlorin from the complex reaction mixture is described later.

A systematic study was made of variations in the preparative method with the object of improving the yield. These are summarised in the Experimental section. Salient points are that the use of the solid ethobromide in place of the free base (VI) reduced the yield of chlorin to 0·1%. Phenetole gave a yield of about 1·5% of a spectroscopically slightly different pigment, perhaps an oxychlorin formed by some process involving oxygen or peroxide (compare p. 3745). The best yield of chlorin (3·9%) was obtained by the action of the Grignard reagent on the free base in boiling *o*-dichlorobenzene.

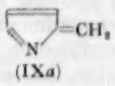
The reaction was also varied by condensing a bifunctional Mannich base, 2 : 5-bispiperidinomethylpyrrole (VII; Bachman and Heisey, *J. Amer. Chem. Soc.*, 1946, **68**, 2496) with pyrrylmagnesium bromide in boiling xylene. Magnesium chlorin was again formed but not in improved yield. Attempts to prepare the unknown 2 : 5-bisdimethylaminomethylpyrrole (VIII) yielded an impure product from which the picrate of the desired base was isolated. The base itself was not obtained pure, or in useful amount.

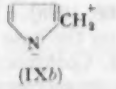

(VII)

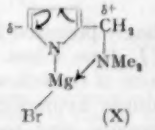

(VIII)

Attempts to use other sources of the linking methine group were uniformly discouraging. The action of gaseous formaldehyde on pyrrylmagnesium bromide in boiling xylene failed to give any macrocyclic pigment, which is not surprising as Taggart and Richter (*J. Amer. Chem. Soc.*, 1934, **56**, 1385) have shown that the primary product is 1-hydroxymethylpyrrole. Neither could any chlorin or porphin be obtained from 2-hydroxymethylpyrrole (Silverstein, Ryskiewicz, and Chaikin, *J. Amer. Chem. Soc.*, 1954, **76**, 4485), a compound which is extremely sensitive to acids. Its reaction with ethylmagnesium bromide in boiling xylene failed to give any macrocyclic pigment.

A few comments can be made on the mechanism of the production of chlorin from the Mannich bases, but these must be offered with reserve because of the low overall yield.


(IX*a*)

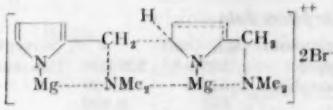

(IX*b*)


(X)

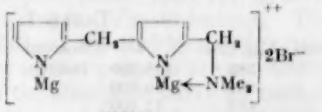
Hellmann (*Angew. Chem.*, 1953, **65**, 473) has suggested that the *C*-alkylation of a pyrrolic Mannich base can go through an unsaturated pyrrolenine form (IX*a*) which can then react with a compound containing an active hydrogen by Michael-type addition. Alternatively, the intermediate could be written in the extreme ionised form (IX*b*) in which case *C*-alkylation would proceed by reaction with a carbanion. Cookson and Rimington (*loc. cit.*) have

used a similar mechanism to explain the formation of uroporphyrin from porphobilinogen (V).

For the self-condensation of a Grignard derivative of a Mannich base we suggest that the intermediate has the structure (X) and that *C*-alkylation and base elimination take place by a concerted process yielding the product (XII) through a transition state such as (XI):



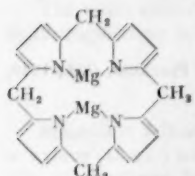
(XI)



(XII)

The product (XII) can react with another molecule of (X) to build up a linear tripyrryl intermediate and by a further step a linear polymer or a macrocycle, such as (XIII). The latter being at the unstable porphyrinogen reduction level would easily be dehydrogenated. The prevailing reaction conditions do not correspond to a very high oxidising potential and the process stops at the chlorin level, although, as is shown below, a little porphin is formed.

In connection with the proposed mechanism it is interesting that the Mannich base (VI) can also react with aluminium chloride to give a little chlorin. The aluminium chloride acts as a Lewis acid. Boron trifluoride, although it failed to give a macrocycle, gave highly coloured materials very possibly linear in structure.



(XIII)

Purification and Properties of Chlorin.—The product of the reaction between ethylmagnesium bromide and the base (VI) was a complex mixture containing at least four pigments. The solvent used in the reaction was first removed under reduced pressure and replaced by benzene, after which the complex was decomposed with 1% hydrochloric acid. Attempts to purify the metal-free chlorin at this stage by adsorption chromatography failed.

Counter-current distribution was found to be a much more satisfactory method. Chlorin could be obtained nearly pure, contaminated only with a little porphin, by successive distributions in a Craig machine (Weissberger, "Techniques of Organic Chemistry," Interscience, New York, 1950, Vol. III, Ch. 4), first between benzene and 3% hydrochloric acid, then between benzene and 10% hydrochloric acid. In the first series of operations, the chlorin remained in the benzene layer whilst the 3% acid retained a small amount of porphin and a brilliant red pigment.* At the second stage the chlorin passed into the 10% acid, whilst the benzene retained another pigment very similar to chlorin in spectrum and differing only in its lower basicity. We have not yet succeeded in obtaining this "pseudo-chlorin" pure. It may be an oxychlorin analogous to the compounds investigated by Pruckner (*Z. phys. Chem.*, 1941, **188**, *A*, 41). The application of counter-current distribution to the purification of chlorin has some analogy with the recent work of Granick and Bogorad (*J. Biol. Chem.*, 1953, **202**, 781) who separated mixtures of porphyrins between ether and dilute acid (compare also Treibs and Schmidt, *Annalen*, 1952, **577**, 105).

The chlorin from the counter-current procedures still contained traces of porphin and minute amounts of the "pseudo-chlorin." Final purification was achieved by partition chromatography on cellulose, light petroleum–*n*-butanol–2N-hydrochloric acid being used as eluant. After crystallisation from benzene the chlorin was then spectroscopically and analytically pure and unchanged by further processing.

Chlorin is a deep bluish-green crystalline solid. It is soluble in benzene, ether, chloroform, and pyridine; insoluble in alcohol, acetone, and water. The solutions are green

* The identity of this material has not been established. We think it very possible that it is based on a pyrrole indigo type of structure, with two pyrrole rings directly joined by a double bond. It has a striking resemblance in light absorption to compounds of this type now under study in these laboratories (Elvidge, J. S. Fitt, and Linstead, unpublished).

with an intense red fluorescence. The solution in dilute hydrochloric acid is blue with an absorption band at 630 mμ. The acid number (Fischer and Kirstahler, *Z. physiol. Chem.*, 1931, **198**, 47) is about 5.

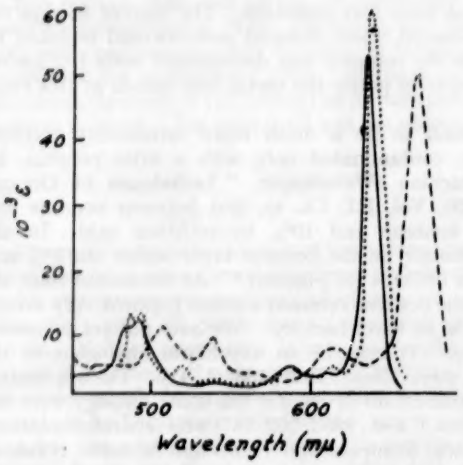
The light absorption of chlorin has been measured in benzene solution over the range 350—700 mμ. The results are given in detail in Table 1 and the typical five-banded spectrum is shown in the Figure.

TABLE 1. *Light-absorption data.*

Compound	$\lambda_{max.}$ (mμ)	ε	Solvent	Ref.	Compound	$\lambda_{max.}$ (mμ)	ε	Solvent	Ref.
Chlorin	388 *	128,000	Benzene	*a*	Copper porphin	393·5 *	329,000	Benzene	*a*
	484	10,600				517·5	13,000		
	493	12,400				552	9,800		
	540	1,300			Copper porphin	518	14,100	Dioxan	*b*
	588	3,600				551·5	8,300		
	610	2,700			Ætiochlorin	488	13,200	Dioxan	*c*
	637·5	50,000				494	13,400		
Magnesium chlorin	402 *	309,000	Benzene	*a*		519	4,200		
	507·5	5,200				522	4,100		
	566	7,700				542	1,800		
	574·5	7,700				564	1,200		
	610	56,000				586	4,000		
Copper chlorin	396 *	195,000	Benzene	*a*		613	4,100		
	490	5,300				642	59,400		
	560	8,200							
	602·5	48,900							

* Soret band.

References: *a*, This work. *b*, Stern, *Z. phys. Chem.*, 1936, **177**, *A*, 58. *c*, Pruckner, *ibid.*, 1940, **187**, *A*, 257.

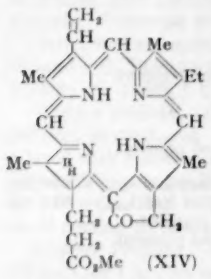


Absorption spectra of chlorins:
——— *chlorin.*
. . . . . *ætiochlorin.*
– – – – – *methyl pyrophæophorbide-a.*

When a benzene solution of chlorin was heated with methanolic cupric acetate it yielded copper chlorin which separated from its blue solution in purple crystals. Light-absorption data are in Table 1. An attempted preparation in boiling acetic acid led to dehydrogenation and the formation of mainly copper porphin, which was characterised by analysis and light absorption (Table 1). Copper chlorin was also easily dehydrogenated to copper porphin in hot hydrochloric acid. Fischer, Platz, Helberger, and Niemer (*Annalen*, 1930, **479**, 27) attempted to prepare the copper derivative of ætiochlorin in acetic acid solution. The light absorption data recorded for their product indicate that it was a mixture containing largely copper ætioporphyrin, which is not surprising in view of our results on the parent compound. Ethylmagnesium bromide reacted with chlorin to yield a solution with an intense magenta fluorescence. The light-absorption data (Table 1) make it

highly probable that this contained magnesium chlorin. The isolation of the pure magnesium pigment was not attempted.

The structure of chlorin (II) is indicated by the analytical data which correspond to $C_{20}H_{16}N_4$; the presence of two atoms of hydrogen in this molecule replaceable by bivalent metal to give $C_{20}H_{14}N_4M$; and the close resemblance to Fischer's chlorins, which is illustrated in the Figure. It will be seen there that the light-absorption curves for chlorin and ætiochlorin (Pruckner, *Z. phys. Chem.*, 1940, **187**, *A*, 257) in the visible region are almost identical in the main features. The weak doublets at about 520 and 564 mμ reported by Pruckner for ætiochlorin have no counterpart in the spectrum of our chlorin.



(XIV)

The Figure also includes the absorption curve for methyl pyro phæophorbide-*a* (Ficken, Johns, and Linstead, unpublished). The accepted formula for this compound is (XIV). (This is based on Fischer's work and neglects questions of fine structure.) This substance is a simplified phorbide derived from chlorophyll and retains the extra hydrogen atoms. There is a good agreement between the general features of the curves for methyl pyrophæophorbide-*a* and for chlorin. In the phorbide the maxima of the main bands are displaced about 25 mμ towards longer wavelengths, owing to the additional substitution.

The main evidence for the structure of chlorin lies in its ready and nearly quantitative dehydrogenation to porphin. This is dealt with in the following paper.

Experimental

Microanalyses are by Mr. Oliver of this Department.

Reaction of 2-Dimethylaminomethylpyrrole (VI) *with Cuprous Chloride.*—The base (VI) (1·2 g.) in xylene (15 c.c.) was added to cuprous chloride (1 g.) in boiling xylene (10 c.c.) during 3·5 hr. The solution was boiled for a further 2 hr., cooled, and filtered. The residual solid was continuously extracted (Soxhlet) with boiling benzene. The benzene extracts and the original filtrate were concentrated under reduced pressure and chromatographed on alumina (grade I). Benzene eluted a pink band which had absorption maxima at 395, 519, and 552 mμ. Evaporation of the benzene solution and crystallisation of the residual solid from chloroform–methanol furnished a red solid (0·5 mg.).

Reaction of (VI) *with Tin Chlorides.*—The base (VI) (1 g.) in xylene (15 c.c.) was treated with stannic chloride (0·4 c.c.) and stannous chloride (0·5 g.). The solution was heated for 18 hr. at 120—130°, cooled, and evaporated to dryness under reduced pressure. The residual solid was continuously extracted with chloroform, and the extracts concentrated and chromatographed on alumina (grade I). A purplish-blue band was eluted with benzene–chloroform (1 : 1), and three arbitrary fractions were collected, having the following absorption maxima: (i) *610*, 564, 506 mμ; (ii) *610*, 535, 565 mμ; (iii) *610*, 535, 568 mμ. Fraction (i) was evaporated to dryness; crystallisation of the residue from chloroform–light petroleum furnished a greenish blue solid (1·3 mg.).

Preparation of Chlorin.—To the base (VI) (1·24 g.) in xylene (50 c.c.) a solution of ethylmagnesium bromide [from magnesium (0·24 g., 1 mol.)] in ether (3 c.c.) was added. The solution was boiled with stirring in an atmosphere of oxygen-free nitrogen for 7 hr., cooled, and filtered. The residual solid was continuously extracted with boiling benzene in an atmosphere of nitrogen. The extracts were mixed with the xylene filtrate from which the xylene had been displaced by benzene, and shaken with cold 1% hydrochloric acid. The yield of chlorin, determined spectroscopically from the band at 637·5 mμ, was 6·7 mg. (0·85%).

The following experiments were done in boiling xylene, ethylmagnesium bromide being added to the base unless otherwise stated.

Expt.	Concn. of (VI) (mole/l.)	Mode of addition	Time of reaction (hr.)	Yield (%) of chlorin
1 *	0·1	All at once at 130°	8	0·8
2	0·04	During 1·5 hr. at reflux	5	1·0
3	0·16	Reverse at room temp.	6	1·0
4	0·07	During 4 hr. at reflux	9	0·86
5 †	0·14	All at once at room temp.	7	0·1

* In presence of excess of ethyl bromide. † Solid ethobromide.

The concentration of the base (VI) was kept at 0·2 mole/l. throughout the following experiments; the reactants were mixed at room temperature.

Expt.	Solvent	Temp.	Time (hr.)	Yield (%) of chlorin	Remarks
1	Xylene	140°	40	0·88	No red pigment
2	,,	,,	24	0·64	Red pigment
3	,,	(*a*) Room temp.	15	—	—
		(*b*) Same expt. continued at 140°	24	1·11	No red pigment
4	Mesitylene	(*a*) 165°	29	1·79	—
		(*b*) Same expt. continued	46	1·11	No red pigment
5	Decalin	190°	6	0	—
6	,,	(*a*) 190°	2·5	0·63	—
		(*b*) Same expt. continued	5	0·54	No red pigment
7	Phenetole	170°	7	1·24	Product had $\lambda_{max.}$ = 640 mμ
8	,, *	,,	29	1·43	Product had $\lambda_{max.}$ = 640 mμ
9	Bromobenzene	155°	23	1·82	Red pigment
10	*o*-Dichlorobenzene	180°	10·5	3·86	No red pigment

* Freshly distilled from sodium.

Reaction of (VI) *with Aluminium Chloride.*—Aluminium chloride (1 g.) in chlorobenzene (50 c.c.) was warmed to 70° with stirring under nitrogen. The base (VI) (1 g., 1 mol.) in chlorobenzene (10 c.c.) was added and the solution was boiled for 10 hr. The resulting dark brown solution had an intense green fluorescence; chlorin was detected spectroscopically but no attempt was made to isolate it. An essentially similar result was obtained in boiling xylene.

Reaction of (VI) *with Boron Trifluoride.*—The base (VI) (1 g.) and boron trifluoride–ether complex (1 c.c., 1 mol.) in xylene (50 c.c.) were boiled for 2·5 hr. in an atmosphere of nitrogen and set aside at room temperature overnight. The resulting deep red solution had a brilliant green fluorescence and showed a faint absorption band at 622 mμ.

2 : 5-*Bisdimethylaminomethylpyrrole* (VIII)—To a solution of dimethylamine hydrochloride (21·63 g., 2·3 mols.) in aqueous formaldehyde (20·11 g., 2·3 mols.), pyrrole (7·75 g., 1 mol.) was added dropwise with stirring at 0° in an inert atmosphere. The mixture was kept for 1 hr. at 0—5°, for 2 hr. at room temperature, and overnight at 0°. It was made alkaline with 20% sodium hydroxide solution and extracted with ether. The ethereal extracts were washed with water and dried ($MgSO_4$), and the solvent removed. Distillation of the residue afforded a forerun, b. p. 71—78°/0·1 mm., and a fraction, b. p. 76—80°/0·15 mm. (1·65 g.), the remainder being non-distillable polymeric material. The distillate partially solidified at 0° affording crystals, m. p. ~30°, which could not be further purified. It was converted into the *picrate* which crystallised from acetic acid in yellow needles, m. p. 202—205° (decomp.) (Found : C, 41·3; H, 4·0; N, 19·6. $C_{22}H_{25}O_4N_8$ requires C, 41·3; H, 3·9; N, 19·7%).

Isolation of Chlorin.—(a) *Attempted adsorption chromatography.* The following adsorbents were too weak to effect a useful separation : grade III alumina; calcium carbonate; calcium hydroxide; sucrose; tartaric acid. Talc, magnesium trisilicate, and grade I alumina all held chlorin too strongly for useful elution. Chlorin was partly decomposed on the last-named adsorbent. When chromatography was tried before demetallation, the magnesium was removed on all the adsorbents tried except sucrose and calcium carbonate; but even on these no satisfactory separation was achieved.

(b) *Counter-current distribution.* The apparatus used in this work was that described by Craig (*Analyt. Chem.*, **1949**, **21**, 500). During the early part of this work an apparatus consisting of 12 tubes with a working capacity of 160 c.c. each was used; later we employed an apparatus with 50 tubes, holding 80 c.c. each. In a typical experiment, the mixed pigments (containing about 50 mg. of crude chlorin in 40 c.c. of benzene) were shaken in the Craig machine with 3% hydrochloric acid. After 15 transfers, tubes 3—8 contained the red pigment ($\lambda_{max.}$ 577, 540 mμ) whilst the chlorin was found in tubes 12—15. The contents of the latter tubes were mixed and made alkaline with ammonia, and the chlorin was extracted with benzene. The benzene solution was concentrated under reduced pressure and the counter-current distribution was repeated with benzene–10% hydrochloric acid. Ten transfers sufficed to separate chlorin (in tubes 1—3) from " oxychlorin " (tubes 8—10). The latter had absorption maxima at 642, 588, and 496 mμ. The general shape of its light-absorption curve was almost identical with that of chlorin.

(c) *Partition chromatography.* The purified chlorin obtained as above was dissolved in a solution obtained by taking the upper phase of an equilibrated mixture of light petroleum (b. p. 100—120°)–*n*-butanol–2N-hydrochloric acid (1 : 2 : 3) and chromatographed on cellulose powder. Elution with the same mixture of solvents effected separation into an upper pink band (porphin) and a lower purple band (chlorin) with a narrow green edge (" oxychlorin "). The purple band was eluted separately and immediately neutralised by a solution of light petroleum–*n*-butanol saturated with ammonia. The resulting solution was washed with water and evaporated to dryness.

After two crystallisations from benzene, *chlorin* was obtained as deep greenish-blue crystals (Found : C, 76·9, 77·2; H, 5·5, 5·5; N, 17·5%; C/H, 14·05, 14·0. $C_{20}H_{16}N_4$ requires C, 76·9; H, 5·2; N, 17·9%; C/H, 14·9).

Copper Chlorin.—Chlorin (10 mg.) in hot benzene (25 c.c.) was treated with cupric acetate (30 mg.) in methanol. The solution was boiled in an atmosphere of nitrogen for 2 min., cooled, diluted with benzene, and washed five times with water. Concentration of the solution afforded *copper chlorin* as small purple crystals which were recrystallised from benzene (Found : C, 64·2; H, 4·15; Cu, 16·1. $C_{20}H_{14}N_4Cu$ requires C, 64·3; H, 3·8; Cu, 17·0%). Chromatography of a small portion on heavy magnesium oxide revealed the absence of copper porphin.

Copper Porphin.—Chlorin (12 mg.) and excess of cupric acetate were boiled in acetic acid (50 c.c.) for 1 hr., no more copper chlorin being then detected in the solution. After removal of the solvent under reduced pressure, the residue was repeatedly extracted with boiling benzene, and the mixed solutions washed with aqueous ammonia and water, and concentrated to small bulk. Chromatography on alumina (grade I) with benzene as eluant afforded *copper porphin* as red microcrystals which were recrystallised from benzene (Found : C, 63·5, 63·95; H, 3·4, 3·9; Cu, 16·3, 16·7. $C_{20}H_{12}N_4Cu$ requires C, 64·6; H, 3·25; Cu, 17·1%).

Magnesium Chlorin.—A solution of chlorin ($\sim 10^{-4}$M; 10 c.c.) in benzene was treated with excess of ethereal ethylmagnesium bromide, and the solution washed with M-ammonium chloride solution (3 times) and water (3 times). It was concentrated to half its volume under reduced pressure and made up to 25 c.c., and the light absorption determined immediately (see Table 1). Aliquots were then converted into chlorin with 1% hydrochloric acid in order to determine its concentration spectroscopically. All operations were carried out with the exclusion of light and air. Solutions of magnesium chlorin were blue with an intense red fluorescence.

We are indebted to Dr. G. E. Ficken for the light-absorption data on methyl pyrophæophorbide-*a* and to Dr. L. M. Jackman for helpful discussions. The work has been made possible by financial support from the Rockefeller Foundation to whom our thanks are due.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [*Received, May 4th,* 1955.]

Chlorophyll and Related Substances. Part II. The Dehydrogenation of Chlorin to Porphin and the Number of Extra Hydrogen Atoms in the Chlorins.*

By ULLI EISNER and R. P. LINSTEAD.

[Reprint Order No. 6390.]

The dehydrogenation of chlorin by various agencies has been studied. The use of quinones of high potential brings about a rapid conversion of chlorin into porphin. The stoicheiometry of this reaction has been studied, and it has been shown that chlorin is a dihydroporphin.

IT is well established, mainly through the work of Conant, Hans Fischer, and Stoll and their collaborators, that the chlorins derived from natural sources are hydroporphyrins. This is true, for example, of the important phorbides of the chlorophyll series, which contain the isocyclic ring connecting the 6- and γ-carbon atoms. It is generally held that the chlorins and phorbides are at the dihydro-level as first postulated for chlorophyll by Stoll and Wiedemann (*Naturwiss.*, 1932, **20**, 706; *Helv. Chim. Acta*, 1933, **16**, 183) but, whilst there is an impressive body of testimony in support of this, it is difficult to find decisive experimental evidence. (For summaries see Linstead, *Ann. Reports*, 1935, **32**, 362; 1937, **34**, 375;

* Part I, preceding paper.

H. Fischer, *FIAT Rev. Biochem.*, **1**, 142; Stoll and Wiedemann, *Fortschr. chem. Forsch.*, 1952, **2**, 538.) Most of the facts could, for example, be reconciled with the interpretation that the chlorins were tetrahydrides, although this would create a consequential problem of structure in the higher hydrides of the bacteriochlorophyll series.

Elementary analysis in compounds of this type is not easy and the results are hardly conclusive. Table 1 summarises the data found for porphin, chlorin, and ætiochlorin.

TABLE 1.

			C, %	H, %	N, %	Total, %	C/H
Porphin	Found :	Fischer and Gleim [1]	77·5	4·8	17·95	100·3	16·08
		Rothemund [2]	77·2	4·8	17·9	99·9	16·08
		Eisner and Linstead [3]	(*a*) 76·7	4·9	—	—	15·53
			(*b*) 76·8	4·8	—	—	15·87
	Calc. for $C_{20}H_{14}N_4$		77·4	4·55	18·06	—	17·03
Chlorin	Found : Eisner and Linstead [3]		(*a*) 76·9	5·47	17·5	99·9	14·08
			(*b*) 77·2	5·52	—	—	13·95
	Calc. for dihydride, $C_{20}H_{16}N_4$		76·9	5·2	17·9	—	14·90
	Calc. for tetrahydride, $C_{20}H_{18}N_4$		76·4	5·8	17·8	—	13·24
Ætiochlorin	Found :	Fischer *et al.*[4]	79·4	8·4	11·9	99·7	9·42
		Schlesinger, Corwin, and Sargent [5]	79·6	8·4	—	—	9·53 (Mean)
			79·5	8·4	—	—	
			79·7	8·3	—	—	
			79·7	8·3	—	—	
	Calc. for ætioporphyrin, $C_{32}H_{38}N_4$		80·3	8·0	11·7	—	10·04
	Calc. for dihydride, $C_{32}H_{40}N_4$		79·95	8·4	11·7	—	9·52
	Calc. for tetrahydride, $C_{32}H_{42}N_4$		79·6	8·8	11·6	—	9·07

[1] *Annalen*, 1936, **521**, 157. [2] *J. Amer. Chem. Soc.*, 1936, **58**, 625. [3] Present work. [4] *Annalen*, 1930, **479**, 27. [5] *J. Amer. Chem. Soc.*, 1950, **72**, 2867.

It will be seen that our chlorin and (particularly) the ætiochlorin of previous workers give figures agreeing better for a dihydride than a tetrahydride. Nevertheless the differences in the theoretical figures are not great, particularly in the ætio-series, and the experimental values tend to run a little high in hydrogen and low in carbon, owing, no doubt, to the obstinate retention of water. (The same trend can be seen in the figures obtained for the three synthetic samples of porphin.) There is therefore some lowering of the experimental C/H ratio (last column); and the results are less precise than could be desired, and are certainly not conclusive. Unequivocal evidence on the hydrogenation level was therefore highly desirable, and we have accordingly studied the dehydrogenation of chlorin.

Early work on the dehydrogenation of more complex chlorins of natural origin involved rather drastic conditions (see Fischer and his co-workers, *Annalen*, 1931, **490**, 84; 1937, **527**, 138; Fischer-Orth, "Die Chemie des Pyrrols," Leipzig, 1937, Vol. II, p. 2). Conant and his co-workers (*J. Amer. Chem. Soc.*, 1931, **53**, 359, 1615, 2382) were the first to study the process quantitatively, for which purpose potassium molybdicyanide was used. Calvin and his associates have recently examined the photo-oxidation of zinc *ms*-tetraphenylchlorin in presence of molecular oxygen or quinones (*ibid.*, 1948, **70**, 699; 1949, **71**, 4024, 4031). Schlesinger, Corwin, and Sargent (*loc. cit.*) have shown that the oxidation of metal-free ætiochlorin with molybdicyanide or ceric sulphate was incomplete even after long periods.

Our work on chlorin showed considerable differences between the ease of dehydrogenation of the metal-free compound and its metallic derivatives, comparable with some of those reported in the literature for more complex chlorins. The ready dehydrogenation of copper chlorin to copper porphin under acid conditions has been mentioned in Part I. The conversion of magnesium chlorin into magnesium porphin is complete within 5 minutes at room temperature on irradiation in the presence of quinones of quite low potential. On the other hand, metal-free chlorin is a relatively stable substance. Its solutions in benzene can be kept indefinitely in the dark and are not affected when molecular oxygen is passed through them for several hours on irradiation. Quinones, however, bring about a smooth dehydrogenation which we have investigated in some detail.

Braude, Jackman, and Linstead (*J.*, 1954, 3548) have shown that the ease of dehydrogenation of 1 : 4-dihydronaphthalene by quinonoid acceptors increases with the potential of the quinone. Braude, Brook, and Linstead (*ibid.*, p. 3569) showed that tetrachloro-1 : 2-benzoquinone and, particularly, 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone, were very powerful dehydrogenating agents for various hydrocarbon donors. Similar effects have now been observed for hydrogen transfers in which chlorin acts as donor. Chlorin was completely dehydrogenated by excess of the following quinones : dichlorodicyano-1 : 4-benzoquinone, 2 minutes at 80°; tetrachloro-1 : 2-benzoquinone, 10 minutes at 130°; but only partially by phenanthraquinone (E° 0·47 v) in 10 hours at 140°.

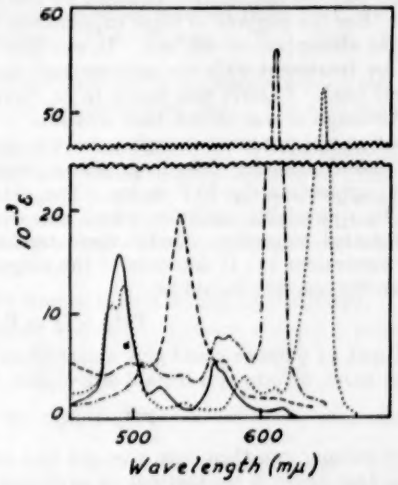


TABLE 2. *Light-absorption data.*

$\lambda_{max.}$ (mμ)	ε	Solvent	Ref.	$\lambda_{max.}$ (mμ)	ε	Solvent	Ref.
Porphin				Magnesium porphin			
395 *	261,000	Benzene	*a*	402 *	487,000	Benzene	*a*
489·5	16,000			497	5,200		
520	3,000			537	19,600		
563	5,200			572	5,400		
568·5 †	4,400						
616	890			491	—	Pyridine–ether	*c*
				535·3			
489	14,800	Benzene	*b*	566			
519	2,500			572·2			
562	4,700			602·5			
615	800						
634	160						

* Soret band. † Inflection.

References : *a*, This work. *b*, Stern, *Z. phys. Chem.*, 1936, **177**, *A*, 58. *c*, Rothemund, *J. Amer. Chem. Soc.*, 1936, **58**, 625.

The reactions between the two powerful quinones and chlorin have been studied quantitatively. It was first established that the reaction product was porphin. When chlorin was heated in concentrations of about 10^{-4} molar for an hour at 130° in boiling chlorobenzene with an excess (2·5 mols.) of tetrachloro-1 : 2-benzoquinone, dehydrogenation was complete and a yield of 61% of crystalline porphin could be isolated. It was characterised by analysis and light absorption and by conversion into the magnesium derivative. Our data (Table 2 and the Figure) for metal-free porphin and its magnesium derivative are in good agreement with those of Stern *et al.* (*Z. phys. Chem.*, 1936, **177**, *A*, 58) and of Rothemund (*J. Amer. Chem. Soc.*, 1936, **58**, 627), respectively.

The stoicheiometry of the dehydrogenation was next examined. For the purpose of estimating the content of chlorin and of porphin in a solution the light absorption was measured at 637·5, 563, and 490 mμ. The first wavelength corresponds with the most important maximum of chlorin in the visible region. Porphin is transparent in this region, and the intensity of absorption accordingly is directly related to the concentration of unchanged chlorin. The absorption at the other two wavelengths, after an appropriate correction for the unchanged chlorin, give values for the porphin formed. In control experiments it was shown that tetrachloro-1 : 2-benzoquinone was decomposed thermally to the extent of about 10% after 2 hours at 130° in boiling chlorobenzene solution and that this figure was not appreciably changed by the presence of the corresponding quinol of or porphin. For the purpose of these experiments the quinone was estimated by making use of its light absorption at 460 mμ. It was also shown that porphin was not appreciably affected by treatment with the quinone and that the reaction was irreversible under the conditions used. Chlorin was found to be thermally stable in chlorobenzene solution at 130°. Although it was shown that solutions of chlorin did not strictly obey Beer's law, the deviation was not great enough to have a significant effect on the results.

The actual transfer dehydrogenations were carried out in boiling chlorobenzene solutions, approximately 10^{-4} molar. The extent of reaction in replicate experiments showed an appreciable variation which was overcome by carrying out the dehydrogenation in sealed ampoules. Under these conditions reproducible results were obtained. Exactly equivalent (1 : 1) amounts of the reagents were used. If chlorin is a dihydride, PH_2, then the reaction should be :

$$PH_2 + Q = P + H_2Q \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Hence 1 mol. of quinone could give a maximum conversion into porphin of 100%. If, on the other hand, chlorin is a tetrahydroporphin, the reaction producing porphin becomes :

$$PH_4 + 2Q = P + 2H_2Q \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

1 mol. of quinone can then only give rise to a maximum conversion into porphin of 50%, provided that there is no thermal or catalysed dehydrogenation not involving transfer.

The results are given in detail in the experimental section. In a reaction period of 1·5 hours about 50% of the chlorin had been decomposed and the mean conversion of this into porphin was 95%. After longer periods dehydrogenation increased, reaching a limiting value of about 70% after 4·5 hours. The mean conversion of chlorin into porphin was slightly lower, being 94% in 3 hours and 92% in 4·5 hours. The departure from the theoretical value is attributed to side reactions involving the decomposition of both the quinone and the porphin as indicated in the blank experiments.

Experiments using a slight (17%) excess of quinone led to an increase in the rate of production of porphin and the ratio, porphin produced/chlorin consumed, nearly approached unity. As was to be expected, a higher proportion of chlorin was dehydrogenated, yielding about 80% of porphin in 3 hours.

Attention was next turned to 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone. The quinone was very unstable, its benzene solution being decomposed to the extent of 30% in 24 hours at room temperature, but since its hydrogenation is much faster than this decomposition, it was possible, by using freshly prepared solutions, to obtain good results for the dehydrogenation of chlorin.

With a 1 : 1 ratio of quinone to chlorin, 80% dehydrogenation was obtained after 3 hours at room temperature or 1 hour at 55°. Conversion of chlorin into porphin was 100%. Longer reaction periods gave a 90% dehydrogenation, which is probably the limiting value in view of the instability of the quinone. We also found that with a 1 : 2 ratio of quinone to chlorin, 50% of the chlorin was converted into porphin, thus confirming the stoicheiometry of dehydrogenation.

All the results were consistent with equation (1) and a dihydride structure for chlorin and quite incompatible with its being a tetrahydride. The close spectroscopic resemblance referred to in Part I provides strong evidence that the natural chlorins are at the same level of hydrogenation, in agreement with current views.

Experimental

Dehydrogenation of Magnesium Chlorin.—Benzene solutions of magnesium chlorin containing 1 : 2-naphtha-, 2-methyl-1 : 4-naphtha-, and 1 : 4-benzo-quinone severally were irradiated with light from a 300-watt bulb. Within 5 min. the magnesium chlorin band at 610 mμ was replaced by a weak diffuse band at 537 mμ due to magnesium porphin.

Preparation of Porphin.—Chlorin (15·3 mg.) and tetrachloro-1 : 2-benzoquinone (30·3 mg., ~2·5 mol.) in chlorobenzene (100 c.c.) were boiled under reflux in an atmosphere of nitrogen for 1 hr.; no more chlorin could then be detected. The cooled solution was extracted with 2N-hydrochloric acid (8 times), and the extracts washed with benzene, basified with ammonia, and extracted with benzene. Concentration of the benzene solution afforded *porphin* (9·4 mg., 61%) which crystallised from benzene in deep reddish-brown platelets (Found: C, 76·7, 76·8; H, 4·9, 4·8%; C/H, 15·5, 15·9. $C_{20}H_{14}N_4$ requires C, 77·4; H, 4·55%; C/H, 17·0). For light absorption, see Table 2.

Magnesium Porphin.—This was prepared in the same way as magnesium chlorin (see Part I) and formed a red solution with a red fluorescence in ultraviolet light. For light absorption, see Table 2.

Dehydrogenation of Chlorin.—(a) *With tetrachloro-1 : 2-benzoquinone.* In the following blank experiments, solutions of the quinone (~10^{-4}M) were boiled in chlorobenzene (i) alone, (ii) in presence of the quinol (1 mol.), and (iii) with porphin (0·5 mol.) and the quinol (1 mol.). The decomposition of the quinone was followed spectroscopically by measurement of the band at 460 mμ. In presence of porphin it was necessary to apply the appropriate corrections for the absorption of the latter.

Percentage of quinone recovered after treatment with boiling chlorobenzene.

Time (min.)	Quinone alone	Quinone + quinol	Quinone + quinol + porphin
25	96·5	99·3	98·0
60	93·6	98·0	94·9
120	89·3	91·3	90·8

It was established that under these conditions porphin remained essentially unchanged and that chlorin was thermally stable.

The following procedure was adopted for the experiments tabulated below. Solutions containing respectively chlorin (6·24 mg./100 c.c.; 1 mol.) and the quinone (4·92 mg./100 c.c.; 1 mol.) in dry chlorobenzene were prepared. Glass ampoules were filled with 1 c.c. of each solution, sealed, and placed in a bath at 130°. After a suitable reaction period the contents of the ampoules were quantitatively transferred to volumetric flasks, the volume made up to 10 c.c. with benzene and the absorptions at 637·5, 563, and 490 mμ were measured. From the first value the percentage of unchanged chlorin was determined; from the last two figures, after the appropriate corrections for the absorption of chlorin, the percentage of porphin formed. It should be pointed out that owing to the relatively low absorption of porphin at 563 mμ the accuracy of results calculated from this wavelength is not very high.

Time of reaction:	1·5 hr.		3 hr.		4·5 hr.	
Unchanged chlorin, %	47·2	47·7	28·4	28·5	26·85	26·75
Porphin formed, % (from 490 mμ band)	50·3	50·3	67·2	65·0	66·25	65·95
Porphin formed, % (from 563 mμ band)	49·05	49·05	67·5	68·3	68·3	68·3
% conversion of chlorin into porphin (490 mμ band)	95·3	92·9	93·9	94·3	90·6	90·0
% conversion of chlorin into porphin (563 mμ band)	96·2	93·8	90·9	95·5	93·4	93·3
Mean conversion	94·55%		93·65%		91·8%	

In the following experiments a 17% excess of quinone was used. The reaction was carried out in 10-c.c. flasks fitted with air condensers, and the time of reaction was 2 hr.

					Mean
Unchanged chlorin, %	18·7	27·7	11·2	23·2	20·2
Porphin formed, % (from 490 mμ band)	74·0	67·7	84·9	75·7	75·6
Porphin formed, % (from 563 mμ band)	82·6	74·5	84·7	75·5	79·3
% conversion of chlorin into porphin (490 mμ band)	91·0	93·5	95·6	98·6	94·7
% conversion of chlorin into porphin (563 mμ band)	101·6	103·1	95·4	98·3	99·6

Similarly, mean values (6 experiments) for a reaction period of 1 hr. were 35·6% unchanged chlorin and 65·9% and 68·3% for porphin formed, representing conversions of 102·3% and 106%, respectively. For a reaction period of 3 hr. (mean of 4 experiments), 17·6% chlorin was unchanged and 79·2% and 82·6% porphin was formed, representing conversions of 97·5% and 100·3%, respectively.

(b) *With* 2 : 3-*dichloro*-5 : 6-*dicyano*-1 : 4-*benzoquinone*. Solutions of chlorin (6·24 mg./100 c.c.; 1 mol.) and the quinone (4·54 mg./100 c.c.; 1 mol.) in dried benzene were prepared and used immediately. 1 c.c. portions of both solutions were sealed into ampoules as described above and kept either in a thermostat at 55° or at room temperature with the exclusion of light.

Temp.	Time, hr.	Unchanged chlorin, %	Porphin formed, % (490 mμ)	(563 mμ)	% Conversion (490 mμ)	(563 mμ)
55°	0·5	24·85	75·0	71·9	99·8	95·7
55°	0·5	24·3	74·35	71·9	98·2	95·0
Room 55°	2 1	15·7	83·55	86·0	99·1	102·0
Room 55°	2 1	14·6	84·9	91·6	99·4	107·2
Room 55°	2 2	12·6	89·2	95·3	102·1	109·0
Room	3	21·6	80·9	85·0	103·2	108·4
Room	20	10·45	91·15	92	101·8	103·8

The following results were obtained from the reaction of 0·5 mol. of quinone with 1 mol. of chlorin.

Temp.	Time, hr.	Unchanged chlorin (%)	Porphin formed (%) (490 mμ)	(563 mμ)	Conversion (%) (490 mμ)	(563 mμ)
55°	1	56·1	41·1	40·4	93·6	92·0
55°	1	54·75	42·5	39·4	93·9	87·1
Room	24	52·0	45·6	45·2	95·0	94·2
Room	24	53·2	43·1	41·35	92·1	88·4

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Studies in Light Absorption. Part XI. Substituted Benzaldehydes, Acetophenones and Related Compounds. The Effects of Steric Conformation on the Electronic Spectra of Conjugated Systems.*

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In conjugated systems X–Y, changes in steric conformation about the single bond can give rise to two types of spectral effects: (1) changes in absorption intensity alone, (2) wavelength displacements of the characteristic electronic bands. Good examples of the first type are provided by alkylated benzaldehydes, acetophenones, cyclic aromatic ketones and related compounds, comprehensive data for which are presented and analysed in detail.

The general discussion of steric effects given previously (Part VI, *J.*, 1949, 1890) is amplified and it is deduced by an application of the Franck–Condon principle that effects of type (1) are produced by transitions between non-planar ground states and uniplanar (or near-planar) excited states, while effects of type (2) are produced by transitions between non-planar ground and excited states. In the former case, the mean interplanar angle θ_1 between X and Y in the ground state is approximately given by $\cos^2\theta_1 = \varepsilon/\varepsilon_0$, where ε_0 is the absorption coefficient expected for the uniplanar system ($\theta_1 = 0$). The values calculated in this way for the angle between the phenyl and the carbonyl group in *o*-alkylated acetophenones and cyclic aromatic ketones agree well with those deduced from dipole moments and scale models (cf. Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117; Braude, *Experientia*, 1955, in the press).

In an earlier paper (Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, Part VI, *J.*, 1949, 1890), the principal types of steric effect encountered in the electronic spectra of conjugated systems were classified into three main classes according to the structural

* Part X, *J.*, 1952, 1069.

conditions by which they are produced. One of these relates to changes due to substituents, such as alkyl groups, which normally cause only relatively minor spectral differences in the near-ultraviolet or visible region. The first examples of this class were discovered by Pickett, Walter, and France (*J. Amer. Chem. Soc.*, 1936, **58**, 2296) in the diphenyl series and many analogous cases were subsequently described by Rodebush and his co-workers (*ibid.*, 1940, **62**, 2906; 1941, **63**, 3018; 1946, **68**, 896) and others. Most of the early observations refer to the almost complete disappearance of a band (*K*-band) characteristic of a conjugated system Ph–X on the introduction of two *o*-methyl substituents into the phenyl ring, often accompanied by the appearance of a new band at shorter wavelength. Thus, 2 : 2′ : 6 : 6′-tetramethyldiphenyl, as well as *o*-ditolyl, show practically no trace of the intense band near 2500 Å of the parent compound, diphenyl, but exhibit new bands near 2200 Å (cf. Beaven, Hall, Lesslie, Turner, and Bird, *J.*, 1954, 131; Braude and Forbes, *J.*, 1955, 3776). The generally accepted interpretation of this type of steric effect [subsequently referred to as type (2)], resulting in a hypsochromic displacement of a *K*-band, is that the *o*-substituents prevent the adoption by the conjugated system X–Y of the uniplanar, or near-planar, conformation required for maximum electronic interaction between X and Y. The *K*-bands of such systems can usually be ascribed to $N \longrightarrow V$ transitions from essentially homopolar ground states to dipolar excited states in which conventional single bonds possess increased double-bond character (cf. Mulliken, *J. Chem. Phys.*, 1939, **7**, 121). As a result, steric hindrance to uniplanarity raises the energy of the excited state more than that of the ground state, *i.e.*, the transition energy increases and $\lambda_{max.}$ is displaced to shorter wavelength. Thus, steric effects of this type involve transitions between non-planar ground states and non-planar excited states.

Another type of steric effect produced by alkyl substituents and other groups of weak conjugating properties is a reduction in the intensity of a *K*-band, without a significant hypsochromic shift. The existence of this kind of effect [subsequently referred to as type (1)] was first recognised in connection with *cyclo*hexene derivatives (Part VI, *loc. cit.*) and many further examples have accumulated during the last five years (cf. Braude and Jones, *J. Amer. Chem. Soc.*, 1950, **72**, 1041; Turner and Voitle, *ibid.*, 1951, **73**, 1403; Oroshnik, Karmas, and Mebane, *ibid.*, 1952, **74**, 295; Henbest and Woods, *J.*, 1952, 1150; Braude, Bruun, Weedon, and Woods, *J.*, 1952, 1419; Farrer, Hamlet, Henbest, and Jones, *J.*, 1952, 2657). The absence of unusual wavelength displacements means that steric effects of type (1) do not significantly alter the transition energy and, since it is highly unlikely that the ground and the excited state would be affected equally, this implies that the separate energy levels are essentially unchanged. Hence, steric effects of type (1) represent a decrease in transition probability alone. An explanation of such phenomena in general terms was put forward in Part VI; it was suggested that, when steric hindrance to uniplanarity is comparatively weak, the relevant transitions might be restricted to those vibrational states of the molecule in which a sufficient degree of planarity is attained. A more detailed interpretation along these lines is given in the sequel. It will be shown by an application of the Franck–Condon principle that steric effects of type (1) can be explained as arising from transitions between non-planar ground states and uniplanar (or near-planar) excited states and that, on certain assumptions, the mean interplanar angle (θ_1) in the ground state can be deduced from the decrease in ε. The analysis of the data in the alicyclic series is rendered more complex by the fact that the two "*ortho*" (*i.e.*, 2 : 6)-positions in *cyclo*hexene derivatives are not structurally equivalent and by the possible existence of two uniplanar *s-cis-trans*-isomers ($\theta_1 = 0°$ and 180°) which would be expected to show different light-absorption properties (cf. Braude and Timmons, Part XII, *J.*, 1955, 3766). This complication is absent in the corresponding phenyl derivatives, and although the earlier work of Rodebush and others was not sufficiently extensive to draw a distinction between the two types of steric effect, the available data indicated that effects of type (1) are also common in the aromatic series. This has now been confirmed by a more detailed investigation of *ortho*-substituted benzaldehydes, acetophenones, and related compounds, and it will be shown that the conformations deduced from the spectral properties are in satisfactory agreement with those which can be derived from measurements of dipole moment and from scale models.

Most of the required compounds were either known or accessible by standard methods which are described in the Experimental section. Some marked discrepancies with the literature were noted in the case of 2 : 6-dimethylbenzaldehyde and 2 : 6-dimethylacetophenone. The aldehyde was prepared by the dehydrogenation of the Diels–Alder adduct of piperylene and crotonaldehyde (Holmes *et al.*, *Canad. J. Res.*, 1948, **26**, *B*, 248) and had m. p. 31°, to be compared with m. p. 11° reported by Lock and Schmidt (*J. prakt. Chem.*, 1934, **140**, 229). The structure of the aldehyde was confirmed by oxidation to 2 : 6-dimethylbenzoic acid, which was converted into 2 : 6-dimethylacetophenone by reaction with excess of methyl-lithium. The ketone formed a 2 : 4-dinitrophenylhydrazone under the usual conditions and its spectral properties are quite different from those recently recorded by Schwartzman and Corson (*J. Amer. Chem. Soc.*, 1954, **76**, 784) for a product which did not yield ketonic derivatives.

Benzaldehydes.—Benzaldehyde exhibits three groups of bands near 2400, 2800, and 3300 Å, designated *K*-, *B*-, and *R*-bands, respectively (*Ann. Reports*, 1945, **42**, 105). The high intensity *K*-band is due to an allowed transition of the benzoyl chromophore which may be represented by Ph–C=O ⟶ $^{+}$Ph=C–O^{-}; the other two bands are of low intensity and are ascribed to forbidden transitions associated with the partial phenyl and carbonyl chromophores. Data for a number of alkylated benzaldehydes (Table 1) show that methyl substituents cause only the usual bathochromic displacements; thus the centres of the *K*-bands are shifted by *ca.* 50 Å and those of the *B*-bands by *ca.* 100 Å to longer wavelengths per methyl group, and the *R*-bands consequently become obscured by the falling branch of the *B*-bands. The bathochromic displacements of the *K*-bands can be ascribed to the effects of the methyl group in facilitating the accommodation of the positive charge in the benzenoid ring, either inductively or by hyperconjugation (cf. Bowden and Braude, *J.*, 1952, 1068; Sweeney and Schubert, *J. Amer. Chem. Soc.*, 1954, **76**, 4625; Burawoy and Spinner, *J.*, 1955, 2085) and they are unaccompanied by any *pronounced* changes in intensity.

Closer inspection, however, reveals that while *m*-methyl substituents cause little change on ε, *p*-methyl substituents produce a small increase (+Δε ~1000), no doubt associated with the electromeric interaction which will be much more effective in the *para*- than in the *meta*-position. *o*-Methyl substituents, however, produce a small, but definite, decrease in ε, although from electronic considerations alone they would be expected to have effects similar to those of *p*-methyl substituents. The ratio ($\varepsilon/\varepsilon_0$) of the observed extinction coefficients to those calculated on the assumption that, in the absence of a special "*ortho*"-effect, *o*-methyl substituents would increase ε by the same amount as *p*-methyl substituents,

TABLE 1. *Ultraviolet-light absorption of alkylated benzaldehydes and their derivatives.*

Ph·CHO derivative	Aldehyde [1] *K*-Band $\lambda_{max.}$ (Å)	*K*-Band ε	*B*-Band $\lambda_{max.}$ (Å)	*B*-Band ε	*R*-Band $\lambda_{max.}$ (Å)	*R*-Band ε	Semicarbazone [2] $\lambda_{max.}$ (Å)	Semicarbazone ε	2 : 4-Dinitrophenylhydrazone [3] $\lambda_{max.}$ (Å)	2 : 4-Dinitrophenylhydrazone ε
Unsubstd.	2420	14,000	2800	1400	3280	57	2810	22,000	3770	28,500 [4]
	2480	12,500	2890	1200	3380	53				
					3530	19				
					3700	6				
p-Me	2510	15,000	2790	1200	3260	30	—	—	—	—
	2570	12,500	*2840*	1000	*3400*	23				
m-Me	2450	13,500	2800	1000	—	—	2840	18,600 [5]	—	—
	2510	12,000	2900	800						
o-Me	2430	12,500	2910	1700	3220	45	2810	17,700	3860	30,600
	2510	13,000					2910	17,300		
2 : 6-Me_2 ...	2510	12,500	2990	1900	—	—	2810	17,600	3800	30,800
	2560	11,500	3040	1800	—	—	2910	16,200		
2 : 4 : 6-Me_3	2640	14,500	3000	2100	—	—	2810	18,500	3860	29,500
							2900	17,800		

[1] In *n*-hexane or *cyclo*hexane. Figures in italics represent inflections. [2] In ethanol. [3] In chloroform. [4] Braude and Jones, *J.*, 1945, 498. [5] Data obtained by Mr. R. L. Erskine.

is 0·86 for *o*-tolualdehyde and shows little further decrease in 2 : 6-dimethyl- and 2 : 4 : 6-trimethyl-benzaldehyde (see Table 3).

The data for the aldehydes by themselves do not allow any certain interpretation of the

ortho-effect. It could be suggested that the *ortho*-effect is due to intramolecular hydrogen-bonding between the carbonyl and an *o*-methyl group, as has been inferred from other evidence (cf. Watson, "Modern Theories of Organic Chemistry," Oxford, 1937; Kadesh and Weller, *J. Amer. Chem. Soc.*, 1941, **63**, 1310). Since only one *o*-methyl group could participate in such hydrogen-bonding, this would be compatible with the observation that the "*ortho*"-effect is almost the same with one as with two *o*-methyl groups. On the other hand, hydrogen-bonding involving C–H bonds is known to be very weak, and would not be expected to have any marked influence on ultraviolet-light absorption. Vibrational spectral properties are much more sensitive in this respect, but the available data are also inconclusive. The Raman carbonyl stretching frequencies decrease in the sequence phenylacetaldehyde (1718 cm.$^{-1}$), benzaldehyde (1700 cm.$^{-1}$), *o*-tolualdehyde (1688 cm.$^{-1}$), and mesitylaldehyde (1687 cm.$^{-1}$) (Saunders, Murray, and Cleveland, *J. Amer. Chem. Soc.*, 1941, **63**, 3121); the change in frequency produced by *o*-methyl groups might be due either to increased conjugation (as indicated by the shift in $\lambda_{max.}$, see above), or to hydrogen-bonding, or to both. However, when considered in conjunction with the data for alkylated acetophenones, the small "*ortho*"-effect in the *o*-methyl benzaldehydes seems very probably to be mainly steric in origin and due to a slight obstruction to the coplanar arrangement of the phenyl ring and the formyl group.

Acetophenones.—The ultraviolet absorption of acetophenone is very similar to that of benzaldehyde and the bands can be interpreted in an analogous manner (Table 2). As before, alkyl groups in any of the three ring-positions cause only the normal bathochromic displacements, which are accompanied for *p*-substituents by a small increase in the intensities of the *K*-band ($+\Delta\varepsilon \sim 1500$). In contrast to results with the benzaldehydes, however, *o*-methyl substituents produce very marked hypochromic effects, with ratios of observed to expected values ($\varepsilon/\varepsilon_0$) ranging from 0·9 to 0·2 (see Table 3). From the fact that the observed intensities of the *K*-bands of acetophenone and 2 : 4-dimethylacetophenone are almost equal, whereas in 2 : 4 : 6-trimethylacetophenone the intensity is reduced to about one-quarter, O'Shaughnessy and Rodebush (*ibid.*, 1940, **62**, 2906) concluded that *two* *o*-methyl substituents are required to produce the effect. The present, more extensive data show, however, that the spectral properties of 2 : 4-dimethylacetophenone are, in

TABLE 2. *Ultraviolet-light absorption of alkylated acetophenones and their derivatives.*

	Ketone [1]						Semicarbazone [2]		2 : 4-Dinitrophenylhydrazone [3]	
Ph·COMe	*K*-Band		*B*-Band		*R*-Band					
derivative	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
Unsubstd.	2430	13,200	2790	1200	*3150*	55	2700	20,400	3800	27,500 [4]
							2780	17,700		
4-Me	2520	15,100	—	—	—	—	2750	19,900 [5]	—	—
2-Me	2420	8700	2810	1200	*3310*	50	2450	11,800	3660	21,400 [6]
	2450	8300					2500	12,200		
							2560	11,800		
2-Bu^n	2420	8100	2820	1100	—	—	2450	11,700	3680	23,900 [6]
	2450	7600	2910	1000						
2 : 4-Me$_2$ ...	2510	14,100	2820	1700	—	—	—	—	3720	24,900
	2560	12,300	2910	1300						
2 : 5-Me$_2$ ...	2450	9900	2960	1800	—	—	—	—	3690	26,700
	2510	8700								
2 : 6-Me$_2$ ...	2510	5600	*2810*	890	—	—	—	—	3600	28,900
	2560	5200	*2900*	740						
2 : 4 : 6-Me$_3$	2420	3600 [7]	2800	400	—	—	—	—	—	—

[1] In ethanol. [2] In ethanol. [3] In chloroform. [4] Braude and Jones, *J.*, 1945, 498. [5] Turner and Voitle, *J. Amer. Chem. Soc.*, 1951, **73**, 1403. [6] Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 607. [7] O'Shaughnessy and Rodebush, *J. Amer. Chem. Soc.*, 1940, **62**, 2906.

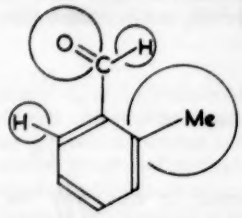
fact, somewhat exceptional and that in 2-methyl- and 2 : 5-dimethyl-acetophenone one methyl substituent is sufficient to decrease ε to about half of the expected value ($\varepsilon/\varepsilon_0$ = 0·58 and 0·66). Actually, 2 : 4-dimethylacetophenone also shows a definite, though smaller, *ortho*-effect, but this only becomes apparent when the increments in ε normally expected for the two methyl substituents are taken into account ($\varepsilon/\varepsilon_0 = 0{\cdot}85$).

The observation that a strong *ortho*-effect is exhibited by acetophenones containing only a single *o*-alkyl substituent supports the conclusion reached above, that intramolecular hydrogen-bonding plays no significant part in these phenomena. If it did, it would be expected that *o*-tolualdehyde and *o*-methylacetophenone would assume the conformations (I*b*) and (III*a*) respectively, and that any resulting spectral abnormality would be the same in both.* The only plausible prime cause of the much larger *ortho*-effect found with the ketones is the large increase in steric hindrance to uniplanarity of the Ph–C=O chromophore when the formyl group is replaced by an acetyl group. This increase can be clearly seen by comparing the projections of the two less-hindered conformations (I*a*) and (III*a*) which show overlap in the ketone but not in the aldehyde, on the basis of the dimensions chosen.

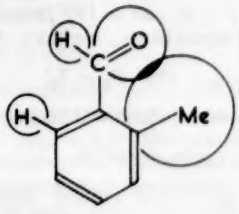
At this point, the choice of radii for scale diagrams requires discussion. In Part VI (*loc. cit.*) the use of covalent in place of the customary van der Waals radii was adopted and briefly justified on the grounds that covalent radii represent a reliable ***minimum*** measure of interference radii between non-bonded atoms belonging to the same molecule, whereas van der Waals radii would predict marked steric effects in many compounds, the ultraviolet-light absorption properties of which are normal. Thus, for example, considerable overlap occurs in acetophenone itself, on the basis of van der Waals radii, between the acetyl group and the *o*-hydrogen atoms, whereas the close similarity between the *K*-bands of benzaldehyde and acetophenone indicates the absence of spectroscopically detectable steric effect in the unsubstituted ketone (cf. footnote, below*). That van der Waals radii are an excessive measure of atomic size even in connection with the stability of optical isomers is apparent from calculations by Stanley and Adams (*J. Amer. Chem. Soc.*, 1930, **52**, 1200). Discussion with several colleagues has shown, however, that our earlier statement that " it is now generally accepted that van der Waals radii represent too large a measure of the intramolecular interference properties of atoms " was not entirely justified. Now, since the repulsion energy between non-bonded atoms is a highly exponential function of distance, the choice of a suitable scale of interference radii is mainly a matter of convenience and will depend on the physical property under investigation. Absorption of ultraviolet light corresponds to energy increments of the order of 100 kcal./mole and the smallest wavelength displacements (*ca.* 50 Å) which are significant in the electronic spectra of organic compounds in solution correspond to energy differences of *ca.* 2 kcal./mole. Thus, ultraviolet-light absorption will be a less sensitive index of steric effects than, for instance, reaction rates where differences of *ca.* 0·1 kcal./mole will be detectable, but a more sensitive index than the existence of isolable optical isomers which requires energy barriers of *ca.* 15 kcal./mole. Now, potential-energy curves for a number of atom pairs (cf. Evans, *Trans. Faraday Soc.*, 1946, **42**, 741; Hill, *J. Chem. Phys.*, 1948, **16**, 399) show that interpenetration energies of the order of 1—3 kcal./mole correspond to distances of approach of about 1 Å less than the sum of the van der Waals radii, a value which is close to the difference between van der Waals and covalent radii. Thus, if no overlap occurs on the basis of covalent radii, steric repulsion will normally amount to less than 3 kcal./mole. Clearly the precise value in any particular case will depend closely on the shape of the potential energy curves concerned and the onset of spectrally detectable steric effects will occur somewhere between the van der Waals and the covalent distances. For the present purpose, it has now been found suitable to represent interference radii as *twice* the covalent radii, *i.e.*, 0·60 Å for hydrogen, 1·70 Å for methyl, and 1·1 Å for doubly bonded oxygen. These values are about *half* the van der Waals radii. (A slightly larger value, 0·75 Å, for hydrogen has been advocated for general purposes by Crombie, *Quart. Rev.*, 1952, **6**, 101.) It will be noted that, with the dimensions chosen, an *o*-methyl group causes no steric overlap with the hydrogen atom of a formyl group, slight overlap with the oxygen atom of a formyl or acetyl group, and considerable overlap with the methyl portion of an acetyl group [See projection (I)—(III)].

* It might be argued that difference arises from steric interference between the acetyl-methyl group and the *o*-hydrogen atom. If such interference existed, it would be expected to operate also in the parent compound, acetophenone, compared with benzaldehyde, whereas the intensities of the *K*-bands are here almost identical. It is partly on this basis that the interference radii have been so chosen as to show no overlap in acetophenone itself.

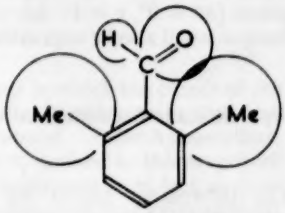
We now return to the main theme. The projection diagrams (I) and (III) indicate that *o*-tolualdehyde and 2-methylacetophenone can assume conformations in which the benzene ring and the carbonyl group are essentially coplanar at the expense of less than *ca.* 3 kcal./mole to overcome steric hindrance. In 2 : 6-dimethylacetophenone (IV) the acetyl-methyl and one of the *o*-methyl groups must overlap, but if the hydrogen atoms were shown separately instead of the solid methyl groups it would be seen that even in this case covalent overlap is comparatively small and the same must obviously be true for all the other aldehydes and ketones in Tables 1 and 2. Hence, whatever the degree of uniplanarity which has to be attained in either the ground or the excited state of the transition



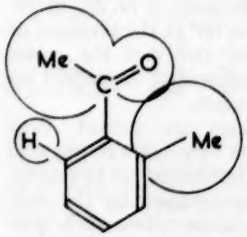
(I*a*)



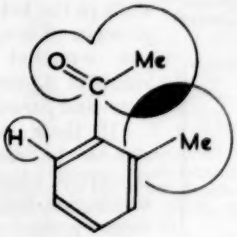
(I*b*)



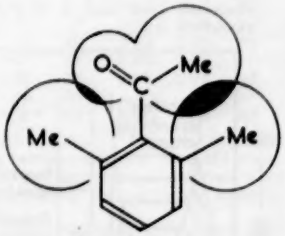
(II)



(III*a*)



(III*b*)



(IV)

Ph–C=O ⟶ $^{+}$Ph=C–O^{-}, any increase in transition energy due to the steric effect of *o*-alkyl substituents will be rather *less* than 3 kcal./mole. No significant hypsochromic wavelength displacements of the *K*-band would therefore be expected, and none are found. The alkylated acetophenones, like their acyclic analogues (Part VI), thus provide an excellent example of relatively weak steric hindrance to uniplanarity which does not result in any appreciable change in $\lambda_{max.}$, and yet results in a marked decrease in $\varepsilon_{max.}$.

The absorption intensity is determined by the transition probability which, in turn, is governed by three things: (i) the selection rules, (ii) the transition moment, which is related to the change in dipole moment in passing from the ground to the excited state; and (iii) the chromophore area (cf. Braude, *J.*, 1950, 379). A steric effect on ε without change in λ cannot be due to a reduction in transition moment, for an $\varepsilon/\varepsilon_0$ ratio of 0·5 or less would then require a highly non-planar excited state, which, as discussed on p. 3755, would in turn be expected to lead to an appreciable change in transition energy. The effective chromophore area will also be little altered by a change in interplanar angle. This leaves only the transition probability, *i.e.*, a change in selection rules resulting in a reduced " allowedness " of the transition, as a likely cause of the decrease in ε. Such a change could come about in the following way (the principle is general though it will be illutrated in terms of the Ph·CO·R system). The upper limit of about 3 kcal./mole deduced for the energy parameter of the steric effect is considerably greater than the spacings of the energy levels of the torsional vibration about the Ph–CO axis of a molecule such as acetophenone. In an *ortho*-substituted, sterically hindered acetophenone, the mean

(equilibrium) angle between the planes of the phenyl and the carbonyl group in the ground electronic state will have some value θ_1 between 0° and 90°, but even at room temperature higher torsional levels corresponding to smaller values of θ will be populated. In the excited electronic state, the mean interplanar angle will have some value θ_2, which will be considerably smaller than θ_1 since the double-bond character of the Ph–CO link is greatly increased. Now, since the motion of electrons is very much faster than that of atomic nuclei (the Franck–Condon principle), the actual angle θ in any individual molecule cannot change during an electronic transition and only those molecules in which $\theta \sim \theta_2$ will be able to undergo the transition (see Fig. 1). The fraction r of all molecules fulfilling this condition will be some function of $(\theta_1 - \theta_2)$. The simplest function which passes through the fixed points ($\Delta\theta = 0°$, $r = 1$; $\Delta\theta = 90°$, $r = 0$; $\Delta\theta = 180°$, $r = 1$) is $\cos^2(\theta_1 - \theta_2)$. Since the fraction r will also be approximately equal to $\varepsilon/\varepsilon_0$, we have : *

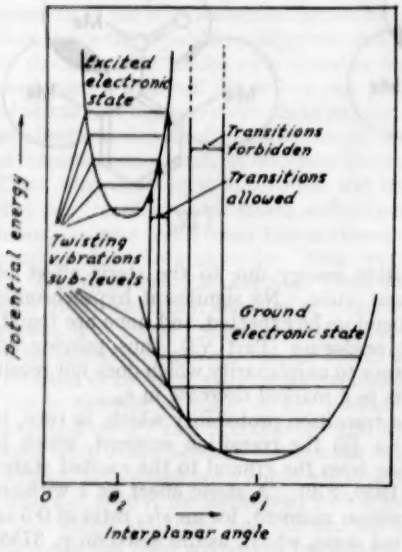
$$\varepsilon/\varepsilon_0 = \cos^2(\theta_1 - \theta_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

or, if we make the additional assumption (which will be justified later) that $\theta_2 \sim 0°$,

$$\varepsilon/\varepsilon_0 = \cos^2 \theta_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The interplanar angles for the electronic ground states derived in this way for *ortho*-alkylated benzaldehydes and acetophenones are given in Table 3 which shows that in the aldehydes, the angle is *ca.* 20° in the presence of either one or two *o*-methyl groups, while in the ketones the angle is *ca.* 35° in the presence of one, and *ca.* 60° in the presence of two, *o*-methyl groups, and that the *actual* values of θ_1 are also somewhat dependent on *meta*- and *para*-substituents.

FIG. 1. *Schematic representation of electronic transitions between a non-planar ground electronic state and a near-planar excited electronic state.*



If these conclusions are correct, they should be confirmed by other physical properties which are influenced by resonance interaction but are conditioned by the electronic ground states alone. Two such properties are vibrational spectra and dipole moments. Only fragmentary data are available for the former, but the Raman carbonyl stretching frequencies of the ketones, in contrast to those of the aldehydes (see above), are increased by *ortho*-alkylation (acetophenone, $\nu = 1684$ cm.$^{-1}$; acetylmesitylene, $\nu = 1699$ cm.$^{-1}$; Sanders *et al.*, *loc. cit.*), indicating that in the ketones the de-coupling effect of the substituents outweighs their conjugative effects. (A detailed study of the infrared spectra, which may be expected to yield more diagnostic information, is being undertaken in these laboratories by Mr. R. L. Erskine.) More extensive data are available on dipole moments (Kadesh and Weller, *J. Amer. Chem. Soc.*, 1941, **63**, 1310; Bentley, Everard, Marsden, and Sutton, *J.*, 1949, 2957; Le Fèvre and Le Fèvre, *J.*, 1950, 1829; Smith, *J.*, 1953, 109). Smith compared the moments of benzaldehyde ($\mu = 2{\cdot}92$ D) and mesitaldehyde ($\mu = 2{\cdot}96$ D) and concluded that there was little or no steric hindrance in the latter, in agreement with the present evidence. The various measurements on acetophenones are not in very

* More precisely, the ratios of the integrated band areas should be used rather than $\varepsilon/\varepsilon_0$. However, the band widths are not markedly affected by alkyl substitution, so that the ratios are not appreciably different.

good agreement, perhaps partly owing to different methods of evaluation, and we shall use the values obtained by Sutton and his co-workers, which are the most complete. In Table 3, the observed dipole moments are given, together with those calculated (μ_0) for the coplanar conformations on the following basis: (i) the moments of methylacetophenones are compounded of the group moments of C=O (taken as 2·96, the value for acetophenone) and C_6H_4–Me (taken as 0·40, the value for toluene, for *o*- and *m*-methyl substituents, and as 0·54, the observed vector component in 4-methylacetophenone, for *p*-methyl substituents); (ii) the vector addition is carried out assuming the carbon–carbon and carbon–oxygen bond angles to be 120°; (iii) for the unsymmetrically substituted ketones, only the less-hindered coplanar conformation is taken into account. The interplanar angle θ_1 can then be expressed by

$$\cos^2\theta \sim (\mu_{obs.} - \mu_{90})/(\mu_0 - \mu_{90}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where μ_{90} is the moment for the completely deconjugated system in which the planes of the phenyl and the carbonyl group are at right angles and which can be taken to be the same as that of a saturated ketone (*i.e.*, $\mu_{90} = 2{\cdot}75$, the value for acetone). Table 3 shows that, except for 2 : 4-dimethylacetophenone, the interplanar angles θ_1 derived in this way from spectral and dipole-moment data are in fair agreement. The agreement is, in fact, as good as could be expected in view of the approximations made and of the fact that expression (3)

TABLE 3. *Steric effects in* ortho-*alkylated benzaldehydes and acetophenones.*

Benzaldehyde derivative	$\varepsilon/\varepsilon_0$ [a]	θ_1 [b]	$\mu_{obs.}$ [c]	μ_0 [d]	θ_1 [e]	Acetophenone derivative	$\varepsilon/\varepsilon_0$ [a]	θ_1 [b]	$\mu_{obs.}$ [c]	μ_0 [d]	θ_1 [e]
Unsubstituted	1·00	0°	2·92	2·92	0°	Unsubstituted	1·00	0°	2·96	2·96	0°
o-Me	0·86	21	—	—	—	2-Me	0·58	40	2·62	2·56	34
2 : 6-Me_2.....	0·78	28	—	—	—	2 : 4-Me_2	0·85	24	2·95	2·83	—
2 : 4 : 6-Me_3 ...	0·85	22	2·96	2·99	15	2 : 5-Me_2	0·66	35	2·85	2·96	46
						2 : 6-Me_2	0·34	55	—	—	—
						2 : 4 : 6-Me_3 ...	0·20 *	63	2·81	3·03	62

[a] Ratio of observed ε of *K*-band to that expected for uniplanar system. [b] Interplanar angle calculated from ε by equation (2). [c] Observed dipole moment (D) in benzene solution (Bentley *et al.*, and Smith, *locc. cit.*). We are indebted to Dr. T. W. Smith for kindly determining and allowing us to quote the value for 2-methylacetophenone. [d] Dipole moment expected for uniplanar system. [e] Interplanar angle calculated from μ by equation (3).

* A lower value of ε (2500) has recently been reported for 95% ethanol (Schubert, Sweeney, and Latovrette, *J. Amer. Chem. Soc.*, 1954, **76**, 5462). This gives $\varepsilon/\varepsilon_0 = 0{\cdot}14$ and $\theta_1 = 67°$.

is very sensitive to uncertainties in μ. Our evaluation of the dipole moment evidence differs in some respects from that of Bentley *et al.* (*loc. cit.*) who employed a slightly different method of estimating μ_0 and, partly on the basis of the abnormal moment exhibited by 2 : 4-dimethylacetophenone, concluded that "a single methyl group is not sufficient to prevent conjugation."

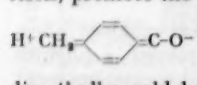
In deducing the simplified expression (2) for the relation between ε and the ground-state interplanar angle θ_1, the assumption was made that the excited state interplanar angle θ_2 is almost zero. This assumption is supported by the fair agreement between the values of θ_1 calculated from the spectral data and from the dipole moment, which is a property of the electronic ground state alone. If the more accurate expression (1) is used, the "spectroscopic" angle actually represents $(\theta_1 - \theta_2)$ and the differences between the second and the fifth column of figures in Table 3 therefore give θ_2. These differences are 6° for 2-methylacetophenone, 11° for 2 : 5-dimethylacetophenone, and 1° for 2 : 4 : 6-trimethylacetophenone, so that θ_2, is, in fact, quite small.

Although, for reasons already discussed, no precise relationship is to be expected between θ_1 and the amount of steric overlap in the planar conformations as indicated by models or scale diagrams, at least a semi-quantitative connection does exist. The rapid increase in overlap in the sequence (*o*-Me : –C–H; negligible) < (*o*-Me : –C=O; slight) < (*o*-Me : –C–Me; marked) explains why, in benzaldehyde, the effect of two *o*-methyl groups is hardly greater than that of one, while in acetophenone the effect is enhanced by a second *o*-methyl group, though not nearly doubled. It is noteworthy that the extent of overlap indicated in the conformation (III*a*) of *o*-methylacetophenone is almost the same as in the

planar conformation of 2 : 6-dimethylbenzaldehyde (II); yet the spectral effect in the mono-*ortho*-alkylated ketone is considerably greater than in the di-*ortho*-alkylated aldehyde. It is possible that, owing to the electron-repelling influence of a methyl group, the effective interference radius of the oxygen atom is, in fact, somewhat larger in an acetyl than in a formyl group and that this accounts for the difference. It also suggests, however, that an appreciable fraction of the molecules of 2-methylacetophenone in the ground state have non-coplanar conformations approaching the more hindered conformation (III*b*) while others have the less-hindered conformation (III*a*), *i.e.*, that the energy levels are sufficiently close for vibrational states with θ_1 differing by 90° to be significantly populated.

The fact that an *o*-butyl group has only a slightly larger effect than an *o*-methyl group (Table 2) is understandable, since all but the first methylene group of the alkyl side chain can assume conformations such that little additional interference is caused. Data for 2-hydroxyacetophenone ($\lambda_{max.}$ 2560 Å, ε 10,500; Morton and Stubbs, *J.*, 1940, 1347; Valyashko and Rozum, *J. Gen. Chem. Russia*, 1946, **16**, 593; 1947, **17**, 755; Dannenberg, *Z. Naturforsch.*, 1949, **4**b, 327) and 2 : 6-dihydroxyacetophenone ($\lambda_{max.}$ 2630 Å, ε 8300; Cram and Cranz, *J. Amer. Chem. Soc.*, 1950, **72**, 595) show that *o*-hydroxyl groups also produce the expected steric reduction in intensity, accompanied by the rather larger bathochromic shifts usual for such substituents (Bowden, Braude, and Jones, *J.*, 1946, 948; Bowden and Braude, *J.*, 1952, 1068). Hydrogen-bonding no doubt also comes into play in this case and accounts, at least in part, for the large spectral differences between the hydroxyl- and methoxyl-substituted ketones (cf. Cram and Cranz, *loc. cit.*). The correlation also holds fairly well when the conjugating group rather than the hindering *o*-substituent is varied (see below). A similar correlation has been noted previously for *ortho*-substituted dialkylanilines by Klevens and Platt (*J. Amer. Chem. Soc.*, 1949, **71**, 1714) who carred out the reverse procedure from that followed here and compared the reductions in absorption intensities (expressed as oscillator strengths) with the interplanar angles deduced from scale models.

Lastly, the rather unexpected influence of *p*-methyl substituents on the magnitude of the *ortho*-effect (see Table 3) deserve comment. In 2 : 4 : 6-trimethylbenzaldehyde and 2 : 4-dimethylacetophenone the *p*-methyl group reduces the *ortho*-effect, whereas in 2 : 4 : 6-trimethylacetophenone it enhances it. A tentative interpretation of these second-order effects is as follows. The mesomeric effect of a methyl group in the *para*-position will, in itself, promote the uniplanarity of the conjugated system owing to the contributions from hyperconjugated structures such as that inset. In 2 : 4 : 6-trimethylbenzaldehyde where the steric obstruction to uniplanarity is quite weak, the interplanar angle is therefore reduced as compared with 2 : 6-dimethylbenzaldehyde. Again, in 2 : 4-dimethylacetophenone the system has the choice of one conformation [corresponding to (III*a*)] in which steric hindrance is weak, and a higher proportion of molecules will approach this conformation rather than the more highly hindered (III*b*) in 2-methylacetophenone. In 2 : 4 : 6-trimethylacetophenone, however, both possible uniplanar conformations are equally hindered, and the additional conjugation merely enhances the congestion at the acetyl group, as compared with 2 : 6-dimethylacetophenone. It may be noted that a 5-methyl group has only a negligible influence on θ in accordance with the fact that the mesomeric effect is only very weakly relayed from the *meta*-position.



Semicarbazones and 2 : 4-Dinitrophenylhydrazones.—Data for these derivatives are included in Tables 1 and 2. As with the parent carbonyl compounds, there is a marked contrast between the effects of *o*-methyl substituents on the characteristic ultraviolet-absorption bands of the aldehydes and ketones. The benzaldehyde derivatives exhibit essentially normal absorption, and methyl substituents produce only the usual, small bathochromic displacements without significant decreases in intensity. This indicates that the interference properties of the –CH=O and –CH=NX [X = NH·CO·NH_2 or NH·$C_6H_3(NO_2)_2$] groups are similar, as would be expected since the covalent radius of nitrogen is slightly smaller than that of oxygen, and since X will lie outside the action radius, at least in the *anti*-stereoisomers (cf. Ramirez and Kirby, *J. Amer. Chem. Soc.*, 1954, **76**, 1037).

The acetophenone derivatives, on the other hand, exhibit markedly abnormal absorption when *o*-methyl substituents are present, but, unlike those for the parent ketones, the bands are displaced to shorter wavelengths as well as decreased in intensity. Thus, the semicarbazone of 2-methylacetophenone has a multiple band located about midway between those of the semicarbazones of acetophenone and of a saturated ketone (cf. $CMe_2{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2$, $\lambda_{max.}$ 2320 Å) and of about half the intensity; and the absorption of the 2 : 4-dinitrophenylhydrazone is typical of that of a saturated ketone (cf. Braude and Jones, *J.*, 1945, 498). Similar observations have been made with oximes and other derivatives by Grammaticakis (*Bull. Soc. chim. France*, 1940, 527; 1947, 664; 1950, 504; *Compt. rend.*, 1950, **231**, 278) and Ramart-Lucas, Hoch, and Vial (*Bull. Soc. chim. France*, 1952, 220; Ramart-Lucas and Hoch, *ibid.*, p. 422). The hypso- and the hypo-chromic effects undoubtedly have the same cause, and the spectral consequences of steric inhibition to coplanarity are evidently different in the ketones and in their derivatives. These observations are analogous to those made with acetyl*cyclo*hexenes and their derivatives (Part VI) and can be interpreted on the basis of the concept of " partial chromophores." In molecules in which the interplanar angle between the Ph– and the –CMe=O or –CMe=NX group is too large to allow the transition characteristic of the full conjugated system, transitions associated with the partial chromophores will have increased probability. If θ reached the maximum value of 90°, partial chromophore bands would have intensities similar to those in systems containing only the separate groups and the absorption would be approximately additive. Now, in the ketones the strong bands expected for the partial –Ph and –CMe=O chromophore are much less intense than the *K*-bands and are at much shorter wavelengths (~2000 Å; cf. Braude, *Ann. Reports*, 1945, **42**, 105), outside the present range of measurements. In the semicarbazones, on the other hand, and particularly in the 2 : 4-dinitrophenylhydrazones, the bands of the full chromophores Ar·CMe=N·X and of the partial chromophores –CMe=NX are of similar intensity and closer together. Thus the multiple band exhibited by the semicarbazone of 2-methylacetophenone (in which, as in the ketone, about half of the molecules in the ground state will have an interplanar angle greater than the critical value) is to be regarded as a superposition of the full and the partial chromophore bands ($\lambda_{max.}$ *ca.* 2700 and 2300 Å) each having about half their usual intensity. In the 2 : 4-dinitrophenylhydrazones, the reversion of the absorption to the partial chromophore type is more complete and it is possible that, owing to the closer proximity of energy levels in these systems, true resonance degeneracy occurs rather than purely geometrical superposition.

Alkyl Phenyl Ketones and Cyclic Aromatic Ketones.—The principles outlined in the previous sections are equally applicable to alkyl phenyl ketones and cyclic aromatic ketones and their derivatives which have been studied particularly by Ramart-Lucas and her school (Ramart-Lucas and Hoch, *Bull. Soc. chim. France*, 1936, 918; 1938, 848, 1001; 1952, 422; Grammaticakis, *ibid.*, 1940, 527; 1941, 427; Biquard, *ibid.*, p. 55; Ramart-Lucas, Hoch, and Vial, *ibid.*, 1952, 220) (Table 4). The absorptions of propiophenone (V) and butyrophenone are almost identical with that of acetophenone and only a slight reduction in ε is noticeable in secondary alkyl phenyl ketones, such as *iso*butyrophenone (VI) and *cyclo*pentyl phenyl ketone; no appreciable hindrance to uniplanarity is expected in any of these cases since the primary or secondary alkyl group can adopt conformations such that they do not interfere with the *o*-hydrogen atom of the phenyl ring. A radically different situation obtains with *tert.*-alkyl phenyl ketones where at least one of the branch-groups must overlap with the *o*-hydrogen atom if the conjugated Ph–C=O system is to be uniplanar. Hence, *tert.*-butyl phenyl ketone (VII) shows a very marked *ortho*-effect and the calculated interplanar angle θ_1 in the ground state is very similar to that deduced previously for *o*-methylacetophenone. The *ortho*-effect increases only slightly in going from *tert.*-butyl to 1 : 1-dimethylpropyl and 1-ethyl-1-methylpropyl phenyl ketone; as with homologous *ortho*-substituents (cf. 2-butylacetophenone) the mere lengthening of an alkyl chain causes only slight extra hindrance since the additional methylene groups can adopt almost non-hindering conformations.

We now turn to the cyclic ketones. The *K*-bands of indanone, tetralone, and related ketones are almost the same, with respect to both $\lambda_{max.}$ and ε, as that of acetophenone,

indicating the the five- and six-membered alicyclic rings permit the carbonyl group to be nearly coplanar with the benzene ring, in agreement with scale models. In benzo*cyclo*hepten-3-one and benzo*cyclo*octen-3-one, however, there is a marked decrease in ε without significant shift in $\lambda_{max.}$ and the interplanar angles calculated by equation (2) are about 40°.

TABLE 4. *Ultraviolet-light absorption and steric effects in alkyl phenyl ketones and cyclic aromatic ketones.**

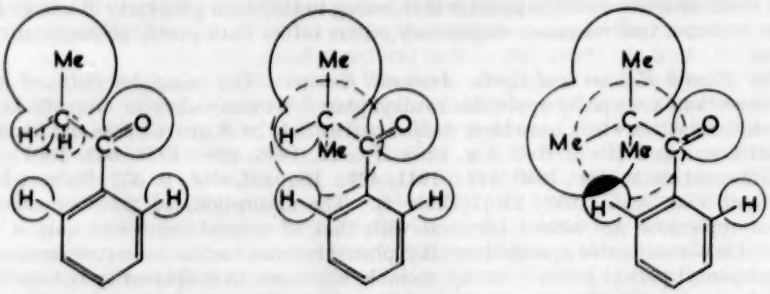
	$\lambda_{max.}$ (Å)	ε	$\varepsilon/\varepsilon_0$	θ_1
Ph·COMe [1]	2420	13,200	1·0	0°
Ph·COEt [1]	2420	13,500	1·0	0
Ph·CO⟨ ⟩ [2]	2380	12,000	0·89	19
Ph·CO·CMe$_3$ [3, 4]	2420	9,100	0·68	34
Ph·CO·CMe$_2$Et [5]	2390	8,300	0·62	38
Ph·CO·CMeEt$_2$ [5]	2380	7,100	0·53	43
Indanone [3, 4]	2430	12,300	0·91	17
1-Tetralone [3, 4]	2480	11,600 †	0·86	22
1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydro-9-oxophenanthrene [6]	2490	11,800	0·87	21
Benzo*cyclo*hepten-3-one [7]	2460	8,100	0·60	39
3 : 4-Benzo-1 : 2-*cyclo*hexano*cyclo*hepten-5-one [8]	2470	7,700	0·57	40
Benzo*cyclo*octen-3-one [4, 7, 8]	2470	6,500	0·48	46
Benzo*cyclo*decen-3-one [8]	2560	11,200	0·85	23

* Most of the data refer to ethanol solutions.

† A lower value (ε 9300) has recently been reported for 95% EtOH (Beyerman, *Rec. Trav. chim.*, 1953, **72**, 550). This would correspond to $\theta_1 = 34°$.

[1] Present work. [2] Braude and Forbes, *J.*, 1951, 1755; Mariella and Raube, *J. Amer. Chem. Soc.*, 1952, **74**, 521. [3] Ramart-Lucas, Hoch, and Vial, *Bull. Soc. chim.*, France, 1952, 220. [4] Heddon and Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 3744. [5] Cram and Knight, *ibid.*, 1952, **74**, 5840. [6] Gutsche and Seligman, *ibid.*, 1953, **75**, 2579. [7] Huisgen and Rapp, *Chem. Ber.*, 1952, **85**, 826. [8] Schubert, Sweeney, and Latovrette, *J. Amer. Chem. Soc.*, 1954, **76**, 5462.

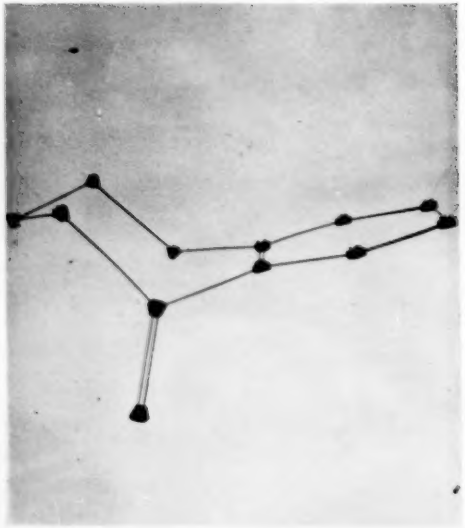
The non-coplanarity here is obviously not due to crowding at the carbonyl function in the same sense as with the open-chain ketones, but is to be ascribed to the effect of the conformation of the alicyclic ring. It can readily be seen with the aid of models that in order that the chain of methylene groups may take up the preferred, staggered zig-zag conformation, the plane of the carbonyl group must be turned out of the plane of the benzene ring, whereas



(V) (VI) (VII)

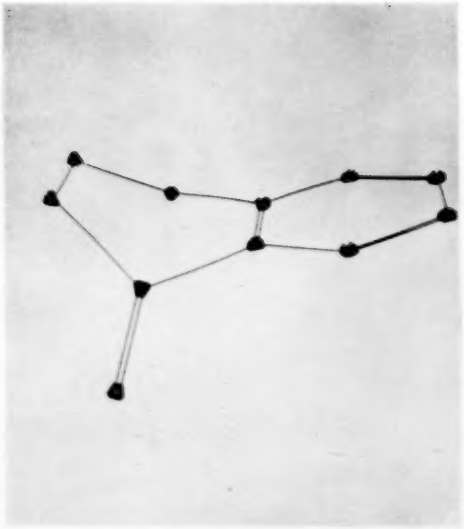
if the chromophore is to achieve uniplanarity, at least one " opposed " conformation must be introduced into the C_4- or C_5-chain. Now, the energy difference between the two corresponding conformations, for example, *n*-butane, is known to be of the same order (3·6 kcal./mole; Pitzer, *Chem. Rev.*, 1940, **27**, 39; Beckett, Pitzer, and Spitzer, *J. Amer. Chem. Soc.*, 1947, **69**, 2488; cf. Turner, *ibid.*, 1952, **74**, 2118) as the Ph–C=O resonance energy, only part of which will, in any case, be lost through non-planarity. It is therefore not surprising that the conformational preference of the alkyl chain prevails over that of the conjugated Ph–C=O system in determining the conformation of the whole molecule. The scale models devised by Barton, which are particularly suitable for this type of problem, indicate (Figs. 2 and 3) that the minimum angles which can be reached in α-tetralone and

FIG. 2



Scale model of benzocyclohexen-3-one (α-tetralone).

FIG. 3



Scale model of benzocycloheptan-3-one.

[*To face p. 3764.*

in benzo*cyclo*hepten-3-one between the phenyl ring and the carbonyl group without undue distortion of the staggered alicyclic ring are about 20° and 40° respectively, in remarkably good agreement with the values of 22° and 39° deduced from the spectroscopic data.

Experimental

Light absorptions were determined with a Hilger–Spekker instrument (Part I, *J.*, 1945, 490). Aldehydes were measured in *n*-hexane; in ethanol, rapid hemiacetal formation occurs even at room temperature. Solutions of acetophenones in ethanol, on the other hand, appear quite stable.

Benzaldehyde had b. p. 179°/769 mm., n_D^{21} 1·5468 (semicarbazone, m. p. 223°). *o*-Tolualdehyde (Law and Perkin, *J.*, 1907, **91**, 258) had b. p. 84—85°/17 mm., n_D^{16} 1·5498 (semicarbazone, m. p. 207—208°; 2 : 4-dinitrophenylhydrazone, m. p. 192—193°). *m*-Tolualdehyde had b. p 83°/16 mm., n_D^{23} 1·5401 (semicarbazone, m. p. 216°). Acetophenone had b. p. 90°/25 mm., n_D^{24} 1·5316 (semicarbazone, m. p. 201°). *p*-Methylacetophenone had b. p. 110°/14 mm., n_D^{21} 1·5531. 2 : 4-Dimethylacetophenone, prepared from *m*-xylene and acetyl chloride (Freund and Fleischer, *Annalen*, 1918, **414**, 5), had b. p. 122—123°/27 mm., n_D^{24} 1·5319 [2 : 4-dinitrophenylhydrazone, m. p. 174° (Norris and Arthur, *J. Amer. Chem. Soc.*, 1940, **62**, 874 give m. p. 174—175°)]. 2 : 5-Dimethylacetophenone, prepared from *p*-xylene and acetyl chloride (Freund and Fleischer, *loc. cit.*) had b. p. 52°/0·1 mm., n_D^{22} 1·5290 [2 : 4-dinitrophenylhydrazone, m. p. 173° (Norris and Arthur, *loc. cit.*, give m. p. 174—175°)].

2 : 6-*Dimethylbenzaldehyde*.—An intimate mixture of 4-formyl-3 : 5-dimethyl*cyclo*hexene (8 g.) (Holmes, Alcock, Demianow, Robinson, Rooney, and Sunberg, *Canad. J. Res.*, 1948, **26**, *B*, 248) and sulphur (4·0 g.) was heated to 280° (bath) under reflux in nitrogen for 12 min.; the vigorous evolution of hydrogen sulphide had then ceased. The once distilled, crude product (5·0 g.) was combined with that (5·8 g.) of a second run and fractionated in nitrogen, giving 2 : 6-dimethylbenzaldehyde, b. p. 230°/762 mm., 118°/27 mm., n_D^{18} 1·548. After crystallisation from pentane (once) and methanol (twice) it was obtained in long needles, m. p. 30—31° (Lock and Schmidt, *J. prakt. Chem.*, 1934, **140**, 229, give b. p. 226°/742 mm., m. p. 11°). The semicarbazone, the formation of which required heating on the steam-bath, crystallised from aqueous methanol as plates, m. p. 167—168° (Lock and Schmidt, *loc. cit.*, give m. p. 158°). The 2 : 4-*dinitrophenylhydrazone* crystallised from dilute ethyl acetate solution as red needles, m. p. 250—251° (Found : C, 57·6; H, 4·85; N, 18·1. $C_{15}H_{14}O_4N_4$ requires C, 57·3; H, 4·5; N, 17·85).

An attempted dehydrogenation of 3-formyl-2 : 6-dimethyl*cyclo*hexene with chloranil in boiling xylene (cf. Bowden and Jones, *J.*, 1946, 52) gave only polymeric material. The structure of the aldehyde was confirmed by oxidation. Potassium hydroxide (2·9 g.) in water (8 ml.) was added, with shaking, to a solution of 2 : 6-dimethylbenzaldehyde (0·90 g.) and silver nitrate (5·3 g.) in water (8 ml.) and ethanol (1·6 ml.). The mixture was heated under reflux on the steam-bath for 30 min. with occasional shaking. After cooling and filtering, the combined filtrates and aqueous washings were acidified and extracted with ether. The ethereal extract was dried (Na_2SO_4) and evaporated, giving crude, solid 2 : 6-dimethylbenzoic acid (0·71 g.), which after sublimation at 20 mm. and crystallisation from water formed needles, m. p. 114—115° (Hufferd and Noyes, *J. Amer. Chem. Soc.*, 1921, **43**, 925, give m. p. 116°).

2 : 4 : 6-*Trimethylbenzaldehyde*.—This was prepared from mesitylene by the method of Hinkel, Ayling, and Morgan (*J.*, 1932, 2797); it had b. p. 116—118°/12 mm., n_D^{21} 1·5531 and solidified at 0°. The semicarbazone crystallised from methanol as plates, m. p. 186°. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate–chloroform as red plates, m. p. 250—251° (Found : C, 58·5; H, 5·1; N, 17·0. $C_{16}H_{16}O_4N_4$ requires C, 58·5; H, 4·9; N, 17·1%).

2-*Methylacetophenone*.—This was prepared from 2-methyl-3 : 6-dihydroacetophenone by dehydrogenation with chromic acid instead of chloranil (cf. Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 607). A solution of chromium trioxide (1·7 g.) and sulphuric acid (2·7 g.) in water (6 ml.) was added dropwise to a cooled solution of the dihydro-compound (3 g.) in acetone (10 ml.). The mixture was kept at room temperature overnight and then diluted with water. The product was isolated with ether and the fraction of b. p. 92—93°/16 mm. was converted to the semicarbazone (1·8 g.) m. p. 198—200°, raised to 204° by crystallisation from ethanol (Auwers, *Annalen*, 1915, **408**, 242, gives m. p. 203°). The semicarbazone was refluxed with light petroleum (50 ml.; b. p. 60—80°) and 2N-sulphuric acid (50 ml.) under nitrogen, with mechanical stirring. After 45 min., the clear petroleum layer was separated, dried, and evaporated, giving 2-methylacetophenone (1·1 g.), b. p. 93°/17 mm., n_D^{23} 1·5235.

2 : 6-*Dimethylacetophenone* [with R. L. Erskine].—A solution of methyl-lithium in ether

(10 ml.) was added to 2 : 6-dimethylbenzoic acid (0·36 g.; prepared as above) in ether (8 ml.). After 1 hr., the mixture was poured into water. The ethereal layer was separated, dried (Na_2SO_4), and distilled, giving 2 : 6-*dimethylacetophenone* (0·22 g.), b. p. 114—116°/21 mm., n_D^{20} 1·5222 (Found: C, 80·75; H, 8·15. $C_{10}H_{12}O$ requires C, 81·05; H, 8·15%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in orange needles, m. p. 154—155° (Found: N, 17·6. $C_{16}H_{16}O_4N_4$ requires N, 17·1%) [Pearson and Greer (*J. Amer. Chem. Soc.*, 1955, **77**, 1294) give m. p. 159°]. Schwartzman and Corson (*ibid.*, 1954, **76**, 784) give b. p. 111°/23 mm., n_D^{20} 1·5162, $\varepsilon < 2000$ at 2500 Å, for the ketone and state that it fails to give a 2 : 4-dinitrophenylhydrazone. In our hands, a sample of their product, kindly provided by Dr. Schwartzman, on treatment with Brady's reagent at room temperature, readily furnished a 25% yield of derivative which, after chromatography on alumina in benzene and crystallisation from benzene had m. p. 223°, $\lambda_{max.}$ 4070 ($E_{1\,cm.}^{1\%}$ 900) and 4450 Å ($E_{1\,cm.}^{1\%}$ 1150) in $CHCl_3$ (Found: C, 52·5; H, 4·5; N, 17·8%; *M*, in camphor, 510).

Most of the experimental work was carried out in 1947—49 while one of us (F. S.) was in receipt of a Senior D.S.I.R. Award which is gratefully acknowledged.

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Studies in Light Absorption. Part XII. The Effects of Steric Conformation on the Ultraviolet and Infrared Spectra of Alicyclic Ethylenic Ketones.*

By E. A. Braude and C. J. Timmons.

[Reprint Order No. 6424.]

The relations between the conformation of the conjugated enone system in alicyclic ethylenic ketones and their electronic and vibrational spectra are discussed. In the ultraviolet, *s-cis-trans*-isomerism affects mainly the intensity, and the interplanar angles θ deduced by the method of Part XI * for 1-acetyl-2-methyl*cyclo*hexene (II) and *tert.*-butyl 2-methyl*cyclo*hexenyl ketone (III), which has been synthesised, agree well with those derived for the benzenoid analogues. In the infrared spectra, *s-cis-trans*-isomerism affects the carbonyl as well as the ethylenic stretching frequencies, and the displacements can be correlated with θ.

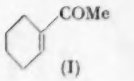
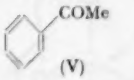
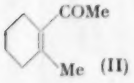
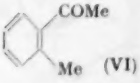
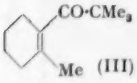
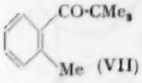
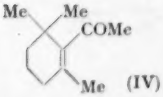
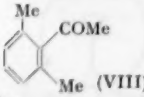
It was shown in Part XI * that steric effects (labelled type I) resulting in a decrease in the intensity of a *K*-band characteristic of a conjugated system without accompanying hypsochromic shift may be ascribed to electronic transitions between non-planar ground states and uniplanar (or near-planar) excited states, and that the equilibrium interplanar angle θ_1 in the ground state may be estimated from the magnitude of the *ortho*-effect on ε. These principles were shown to be readily applicable to *ortho*-substituted acetophenones and related compounds, in which the absorption intensity (ε_0) which the system would have in the absence of steric hindrance to uniplanarity can be accurately assessed. Spectral effects of type (I) are also known to be exhibited by the corresponding tetrahydro-(acetyl*cyclo*hexene) derivatives and it was suggested in Part VI (*J.*, 1949, 1890) that the decrease in ε in 1-acetyl-2-methyl*cyclo*hexene (II) was due to the non-planarity caused by the methyl substituent. If it is assumed that ε_0 would be the same as for the parent compound, 1-acetyl*cyclo*hexene (I), the value of θ_1 calculated from the equation $\cos^2\theta_1 = \varepsilon/\varepsilon_0$ is 44°, practically the same as that deduced for 2-methylacetophenone (see Table 1). Such a result is not unexpected since the geometries of the relevant parts of the two systems are almost identical.

* Part XI, preceding paper.

An alternative interpretation of the difference in the observed absorption intensities of acetyl*cyclo*hexene and 1-acetyl-2-methyl*cyclo*hexene was proposed by Turner and Voitle (*J. Amer. Chem. Soc.*, **1951**, **73**, 1403). They pointed out that ethylenic ketones in which the conjugated system has an enforced *s-cis*-configuration * exhibit considerably lower ε values than analogous compounds with an enforced *s-trans*-configuration, owing to the difference in effective chromophore length and transition moment (Mulliken, *J. Chem. Phys.*, 1939, **7**, 14 *et seq.*). On this basis Turner and Voitle concluded that the chromophores in both 1-acetyl*cyclo*hexene (I) and 1-acetyl-2-methyl*cyclo*hexene (II) are essentially uniplanar, but that whereas the former exists in the *s-trans*-conformation, the latter has an *s-cis*-conformation (II*a*). It seems to us that both interpretations of the spectral data *per se* are equally admissible, but that there are several considerations which favour a non-planar *s-trans*-conformation rather than the planar *s-cis*-conformation for 1-acetyl-2-methyl*cyclo*hexene. The question really is whether the system will be more stable with an interplanar angle θ_1 of about 45° or 180°, the angle being measured with respect to the planar *s-trans*-conformation (II*b*) which, by general consent, has the lowest electronic potential energy (cf. Mulliken, *loc. cit.*).

Now, the absence of significant hypsochromic shifts generally implies (Part XI, *loc. cit.*) that steric hindrance to uniplanarity ($\theta \sim 0°$ or 180°) is quite weak; in the present case, the methyl substituent actually produces the expected small bathochromic shift

TABLE 1. *Steric effects in the light absorption of alicyclic ethylenic ketones and their benzenoid analogues (for references, see text).*

	$\lambda_{max.}$ (Å)	ε	$\varepsilon/\varepsilon_0$	θ		$\lambda_{max.}$ (Å)	ε	$\varepsilon/\varepsilon_0$	θ
 (I)	2320	12500	1·0	0°	 (V)	2420	13000	1·0	0°
 (II)	2450	6500	0·52	44	 (VI)	2420	8500	0·58	40
 (III)	2390	1300	0·10	71	 (VII)	(2360) *	1900	0·14	68
 (IV)	2430	1400	0·11	71	 (VIII)	2510	5500	0·34	55

* Shoulder.

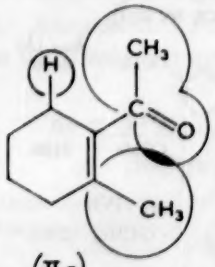
and any compensated hypsochromic displacement must amount to less than 20 Å, equivalent to about 1 kcal./mole. No data are available for the potential-energy difference between planar *s-cis*- and *s-trans*-conformations of the conjugated enone system C=C·C=O, but it seems reasonable to assume that it will be of the same order as for the diene system, C=C–C=C, *i.e.*, *ca.* 2·5 kcal./mole (Aston, Szasz, Woolley, and Brickwedde, *J. Chem. Phys.*, **1946**, **14**, 67). Thus, it seems probable that the conformation with $\theta_1 = 45°$ will have a lower potential energy ($E_0 + 1$ kcal./mole., where E_0 is the energy of the planar *s-trans*-system) than that ($E_0 + 2·5$ kcal./mole) of the conformation with $\theta_1 = 180°$, and that the former will therefore be preferred. A more detailed schematic illustration of the suggested relations is given in Fig. 1. The solid and the broken curve represent the dependence of resonance energy and steric repulsion, respectively, on θ (it is assumed for simplicity that there is no steric hindrance to uniplanarity in the *s-cis*-conformation); since repulsion is a highly exponential function of non-bonded interatomic distances it will be much more sensitive to θ than will resonance, and decrease more rapidly as θ changes

* We use the terms " configuration " and " conformation " respectively in connection with stereoisomerism involving energy barriers greater and smaller, respectively, than *ca.* 20 kcal./mole.

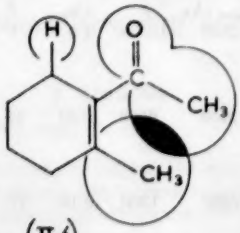
from 0° to 90°. The difference between the curves for any value of θ represents the stabilisation energy for that particular conformation and the Figure depicts conditions under which this is greater for $\theta = 45°$ (intercept *a*) than for $\theta = 180°$ (intercept *b*).

Some support for these views is provided by the close agreement between the interplanar angles calculated on this basis for 1-acetyl-2-methyl*cyclo*hexene and 2-methylacetophenone. There is no question that the *ortho*-effect in the latter is due to non-planarity and not to *s-cis-trans*-isomerism, since the chromophores of the two possible planar conformations (VI*a*) and (VI*b*) are identical (unless a high degree of asymmetry in the electron-distribution in the benzenoid ring is postulated). The possible ambiguity in the interpretation of the ultraviolet-light absorption of 1-acetyl-2-methyl*cyclo*hexene arises partly from the (as we believe, accidental) similarity between the ε value exhibited by this compound and by alicyclic ethylenic ketones with an enforced *s-cis*-configuration. Any further reduction in ε which might be observed in other cases would have to be entirely due to non-planarity. In order to provide a test case of this type and to demonstrate further the parallelism between the alicyclic and benzenoid series, we synthesised *tert.*-butyl 2-methyl*cyclo*hex-1-enyl ketone (III) for comparison with its analogue, *tert.*-butyl *o*-tolyl ketone (VII) which has been described by Ramart-Lucas, Hoch, and Vial (*Bull. Soc. chim. France*, 1952, 220), and exhibits a *K*-band of exceptionally low intensity (see Table 1).

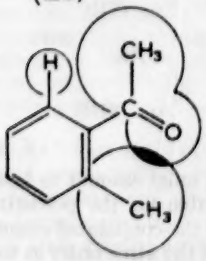
Preparation of the ketone (III) was first attempted by the Friedel–Crafts reaction between 1-methyl*cyclo*hexene and pivalic anhydride in the presence of stannic chloride



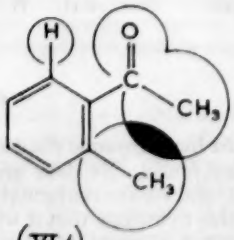
(II*a*)



(II*b*)



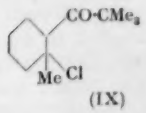
(VI*a*)



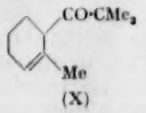
(VI*b*)

by analogy with the methods previously employed for 1-acetyl-2-methyl*cyclo*hexene (cf. Part VI, *loc. cit.*; Royals and Hendry, *J. Org. Chem.*, 1950, **15**, 1147). Dehydrochlorination did not occur during the working-up procedure—contrast the latter case—and the chloro-ketone (IX) was obtained in 60% yield. This was unaffected by refluxing diethylaniline, but on treatment with alcoholic potassium hydroxide afforded an ethylenic ketone which showed high-intensity absorption rising to a maximum below 2100 Å and was evidently the unconjugated isomer (X) of the desired ketone (III). It is interesting that in the case of the lower homologue, acetylmethyl*cyclo*hexene, where the desired product is less highly hindered, a mixture of the corresponding conjugated and unconjugated ketones is obtained (Part VI, *loc. cit.*).

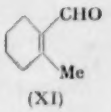
However, 1-formyl-2-methyl*cyclo*hexene (XI) and *tert.*-butylmagnesium chloride gave the crystalline alcohol (XII) which was converted into the ketone (III) by oxidation with active manganese dioxide. This ketone was a liquid which, like its benzenoid analogue (Ramart-Lucas *et al.*, *loc. cit.*), did not form carbonyl derivatives under the usual conditions, but was shown to be substantially free from unchanged alcohol and unconjugated isomers



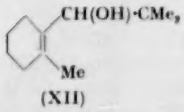
(IX)



(X)



(XI)



(XII)

by its infrared spectrum. Its ultraviolet-light absorption shows a *K*-band at almost the normal wavelength, but of extremely low intensity, similar to that recorded for *tert.*-butyl *o*-tolyl ketone (see Table 1).

It may be noted that both ketones (III) and (VII) show small bnt definite hypsochromic shifts ($\Delta\lambda$ *ca.* -50 Å) with respect to the corresponding methyl ketones. These shifts

FIG. 1. *Dependence of resonance energy and repulsion energy on interplanar angle (schematic).*

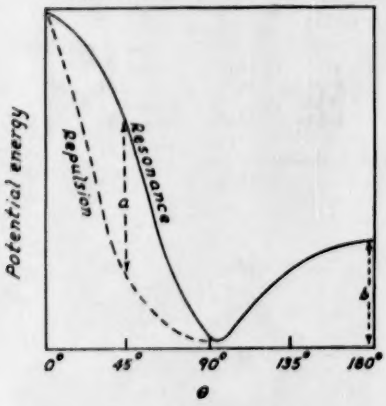
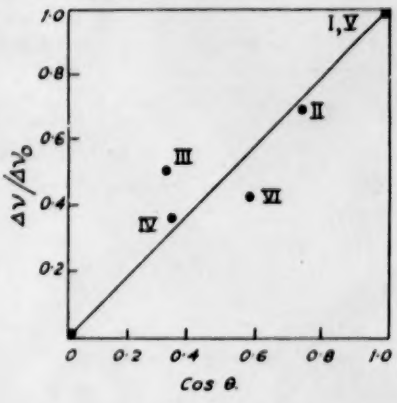


FIG. 2. *Relation between interplanar angle and relative carbonyl stretching frequency shifts in acetylcyclohexenes and acetophenones.*



are almost certainly steric in origin rather than due to differences in hyperconjugation, and represent an energy change of *ca.* 3 kcal./mole; they indicate that the very marked increase in steric hindrance in going from the methyl to the *tert.*-butyl ketones very nearly causes a change-over from type (1) to type (2) steric effects (Part XI, *loc. cit.*).

Since the present work was commenced, another alicyclic ethylenic ketone showing a *K*-band of exceptionally low intensity, 1-acetyl-2 : 6 : 6 : trimethyl*cyclo*hexene (IV), has been described (Henbest and Woods, *J.*, 1952, 1150). This can be compared with 2 : 6-dimethylacetophenone (VIII), but, unlike the other two cases, the calculated interplanar angle is rather larger than for the benzenoid analogue (see Table). The lower intensity of absorption and the greater non-planarity of the alicyclic ketone in this instance is, no doubt, due to the presence of two methyl groups in the 6-position; although only one of these is " quasi "-equatorial (cf. Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21) and is the main cause of interference, models show that the other " quasi "-axial methyl group also contributes to the steric effect.

It is of interest that the progressive increase in interplanar angle in the sequence (I) < (II) < (III), (IV) deduced from the differences in ultraviolet-light absorption is also reflected in the infrared spectra, particularly the carbonyl stretching frequencies (Table 2). The location of the carbonyl band of the methyl ketone (I) is normal for a

conjugated ethylenic ketone, whereas the location of the carbonyl bands of the hindered ketones (III) and (IV) approaches that of saturated ketones. This is clearly a consequence of the reduced extent of effective conjugation in the hindered, non-planar compounds, but it will be noted that while the main change in the electronic spectra is only in intensity, the vibrational spectra show a change in frequency (*i.e.*, wavelength). Analogous effects are shown in the acetophenone series by the Raman carbonyl stretching frequencies (Part XI, *loc. cit.*) and an approximately linear relation appears to exist between the interplanar angle θ_1 and $\Delta\nu/\Delta\nu_0$ where $\Delta\nu$ refers to the shift with respect to an unconjugated ketone (taken as 1707 cm.$^{-1}$) and $\Delta\nu_0$ to the shift in the unsubstituted uniplanar compound (Fig. 2). Somewhat similar observations have also been recorded recently by Crombie (*J.*, 1955, 1007) with conjugated diene systems.* The phenomenon may well prove to be general and it may be qualitatively interpreted as follows. Electronic interaction, which controls resonance energy in the ground state and transition energy in electronic spectra, is a relatively insensitive function of interplanar angle, especially at low values of θ (cf. Guy, *J. Chim. phys.*, 1949, **46**, 469), and hence considerable non-planarity can be tolerated without significant changes in wavelength, although the intensity is decreased (type I steric effects, Part XI). By contrast, mechanical interaction, which controls force constants and transition energy in vibrational spectra, is a more highly

TABLE 2. *Infrared spectra of alicyclic ethylenic ketones.*

Ketone	$\nu_{C=O}$ (cm.$^{-1}$)	ν/ν_0	$\nu_{C=C}$ (cm.$^{-1}$)	$\nu_{C=O} - \nu_{C=C}$ (cm.$^{-1}$)
(a) With labile s-*conformation.*				
(I) [1]	1665	1·0	1637	28
(II) [1]	1678	0·69	1621	57
(III) [2]	1684	0·55	—	—
(IV) [2]	1693	0·33	1650	43
(b) With fixed s-trans-*configuration.*				
[1]	1680	—	1626	54
[1]	1665	—	1629	36
[1]	1661	—	1626	35
Cholest-1-en-3-one [4]	1680	—	1605	74
Cholest-4-en-3-one [4]	1674	—	1615	59
Methyl 3-hydroxy-12-oxochol-9 : 11-enoate [4]	1680	—	1607	73
(c) With fixed s-cis-*configuration.*				
7-Oxoergosta-8(14) : 22-dien-3-yl acetate [3] *	1680	—	1589	91
15-Oxocholest-8(14)-en-3β-yl acetate [3] *	1705	—	1625	80
15-Oxoergosta-8(14) : 22-dien-3-yl acetate [3] *	1697	—	1620	77

[1] This paper (liquid film). [2] This paper (in CCl_4). [3] Henbest and Woods (*loc. cit.*) (in CCl_4). [4] Jones, Humphries, Packard, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 86; Jones, Humphries, and Dobriner, *ibid.*, p. 956; Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252. (In CS_2 and $CHCl_3$.)

* We are much indebted to Professor D. H. R. Barton, F.R.S., for kindly supplying samples of these compounds (Barton and Laws, *J.*, 1954, 52).

sensitive function of interplanar angle in a coupled system, and hence non-planarity has a more immediate effect on frequency. Further work is in progress to test the quantitative aspects of these matters.

Significant displacements are also observed in the ethylenic stretching frequencies. Like the carbonyl stretching frequencies, these are smaller by *ca.* 60 cm.$^{-1}$ than for isolated

* We are indebted to Dr. L. Crombie for kindly communicating his results in advance of publication.

double bonds, showing that the decrease in the force constants arising from conjugation is about equal for the C=O and C=C groups. Examination of a number of ethylenic ketones in which the configuration of the conjugated system is fixed reveals the interesting fact, however, that the location of the C=C stretching frequency depends markedly on whether the conformation is *transoid* or *cisoid* (Table 2). For three *transoid* examples, $\nu_{C=C}$ is 1627 ± 2 cm.$^{-1}$, whereas for the *cisoid* 7-oxergost-8(14)-ene derivative, $\nu_{C=C}$ is considerably smaller. This difference is not unexpected, since the stronger dipole interaction in the *cisoid*-system (A) than in the *transoid*-system (B) should result in an additional

decrease in the force constant of the stretching vibration. Higher ethylenic as well as carbonyl stretching frequencies are exhibited by the two 15-oxo-8(14)-stenyl derivatives; these anomalies appear to be associated with ring-strain in these positions, similar, though opposite in sign, to the effects observed with isolated ethylenic bonds (Henbest, Meakins, and Wood, *J.*, 1955, 800). The differences between the ethylenic and carbonyl stretching frequencies are, however, consistently greater for *s-cisoid* (> 75 cm.$^{-1}$) than *s-transoid* (< 75 cm.$^{-1}$) derivatives. The close correspondence between the ethylenic stretching frequency of 1-acetyl-2-methyl*cyclo*hexene and those of enone systems with a fixed *s-trans*-configuration may be adduced as further support for the view that, at least under the conditions of the spectroscopic measurements, 1-acetyl-2-methyl*cyclo*hexene exists predominantly in a hindered *s-trans*- rather than in a *s-cis*-conformation.

Experimental

M. p.s were determined on a Kofler micro-m. p. block and arecorrected. Analytical data were determined by Mr. F. H. Oliver and the staff of the microanalytical laboratory of this Department.

Ultraviolet-light absorptions were determined by Mrs. A. I. Boston using Hilger–Spekker and Unicam instruments. Infrared data were determined by Dr. E. S. Waight and Mr. R. L. Erskine using Grubb-Parsons single-beam and double-beam instruments.

1-*Formyl*-2-*methyl*cyclo*hexene* (XI).—5-Formyl-4-methyl*cyclo*hexene was prepared in 200-g. batches by heating a stirred mixture of butadiene (310 g.), freshly distilled crotonaldehyde (278 g.), and quinol (4 g.) in an autoclave at 150° for 5 hr. (cf. Diels, Alder, Lübbert, Navjoks, Querberitz, Röhl, and Segeberg, *Annalen*, 1929, **470**, 62; Shortridge, Craig, Greenlee, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1948, **70**, 946). Fractionation of the product through a 14" Fenske column gave the aldehyde, b. p. 67°/16 mm., in 39—46% yields (3 experiments).

This product, even after being kept overnight with Raney nickel in methanol, could not be hydrogenated appreciably at atmospheric pressure with palladium black or 5% palladium–calcium carbonate in methanol with or without acetic acid (cf. Diels *et al.*, *loc. cit.*), but reduction proceeded readily in the presence of platinic oxide. The reaction was interrupted after 0·9 mol. of hydrogen had been absorbed. Isolation of the products and fractionation afforded (i) 1-formyl-2-methyl*cyclo*hexane (25%), b. p. 65—73°/15 mm., n_D^{21} 1·4574 (semicarbazone, m. p. 152—155°) (Diels *et al.*, *loc. cit.*, give b. p. 61—62°/11 mm., semicarbazone, m. p. 155°; Skita, *Annalen*, 1923, **431**, 1, gives b. p. 72°/24 mm., n_D^{20} 1·4498, semicarbazone, m. p. 152°, for the *trans*-compound) and (ii) 2-methyl*cyclo*hexylmethanol (52%), b. p. 73—100°/15 mm., n_D^{21} 1·4644—1·4748 (Skita, *loc. cit.*, gives b. p. 192—192·5°, n_D^{20} 1·4665, for the *trans*-compound). The colourless 3 : 5-*dinitrobenzoate*, crystallised from aqueous methanol, had m. p. 69—71° (Found : C, 56·2; H, 5·5; N, 8·7. $C_{15}H_{18}O_6N_2$ requires C, 55·9; H, 5·6; N, 8·7%). The alcohol was oxidised to the aldehyde in 24% yield by chromic oxide in acetic acid (Skita, *loc. cit.*), but not by selenium dioxide in refluxing dioxan (15 hr.).

1-Formyl-2-methyl*cyclo*hexane was converted into 1-formyl-2-methyl*cyclo*hexene by the method of Heilbron, Jones, Richardson, and Sondheimer (*J.*, 1949, 737) and after regeneration from the semicarbazone, m. p. 239—241° (Heilbron *et al.*, *loc. cit.*, give m. p. 232—233°), had b. p.

96—99°/17 mm., n_D^{21} 1·5082, $\lambda_{max.}$ 2420 Å (ε 11,000 in EtOH) (Heilbron *et al.*, *loc. cit.*, give b. p. 103°/27 mm., n_D^{18} 1·5091; Dreiding and Nickel, *J. Amer. Chem. Soc.*, 1954, **76**, 3965, give n_D^{25} 1·5088).

2 : 2-*Dimethyl*-1-(2-*methyl*cyclo*hex*-1-*enyl*)*propan*-1-*ol* (XII).—A solution of the above aldehyde (5·6 g.) in anhydrous ether (10 ml.) was added to a stirred ethereal solution of *tert.*-butylmagnesium chloride (from Mg, 2·2 g., and *tert.*-butyl chloride, 17 g.) at room temperature. Stirring was continued overnight and saturated aqueous ammonium chloride (30 g.) was then added. Extraction with ether and distillation gave the alcohol (5·6 g., 74%), b. p. 67°/0·5 mm., n_D^{22} 1·4868, which solidified and crystallised from aqueous methanol in prisms, m. p. 59—60° (Found : C, 79·0; H, 12·2. $C_{12}H_{22}O$ requires C, 79·0; H, 12·2%). Light absorption in EtOH : ε 4000 at 2100 Å, and ε 1400 at 2200 Å.

tert.-*Butyl* 2-*Methyl*cyclo*hex*-1-*enyl Ketone* (III).—The foregoing alcohol (4 g.) was shaken with a suspension of manganese dioxide (40 g.) in pentane (400 ml.) under nitrogen for 4 days (cf. Braude and Forbes, *J.*, 1951, 1755; 1953, 2208; Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094; Bharucha and Weedon, *J.*, 1953, 1571). Filtration, evaporation of the pentane, and distillation afforded the ketone as a colourless oil (1·2 g., 30%), b. p. 115—116°/20 mm., n_D^{22} 1·4760 (Found : C, 79·7; H, 11·5. $C_{12}H_{20}O$ requires C, 80·0; H, 11·2%). Ultraviolet absorption in EtOH : $\lambda_{max.}$ 2390 (ε 1300) and $\lambda_{infl.}$ ~2900 Å (ε 8·8). Infrared absorption in CCl_4 : $\nu_{max.}$ 1684 cm.$^{-1}$. The ketone did not form an oxime or a 2 : 4-dinitrophenylhydrazone under the usual conditions.

tert.-*Butyl* 2-*Methyl*cyclo*hex*-2-*enyl Ketone* (X).—Pivalic anhydride was prepared by adding pyridine (28 g.) followed by pivalic acid (28 g.) in benzene (28 ml.) to a solution of pivaloyl chloride (36 g.) in benzene (200 ml.) at 5—10° with shaking (cf. Adkins and Thompson, *J. Amer. Chem. Soc.*, 1949, **71**, 2242). The reaction was allowed to proceed at room temperature for 1 hr., after which the precipitated pyridine hydrochloride was filtered off and washed with benzene. The combined benzene filtrates were washed with water and aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and distilled, giving the anhydride (42 g., 75%), b. p. 112—114°/63 mm., n_D^{21} 1·4080 (Greenwood, Whitmore, and Crooks, *J. Amer. Chem. Soc.*, 1938, **60**, 2028, give b. p. 124°/93 mm., n_D^{20} 1·4093; Conn, Kistiakowsky, Roberts, and Smith, *ibid.*, 1942, **64**, 1747, give b. p. 95·0°/28 mm.).

The anhydride (45 g.) was added in drops to a stirred mixture of methyl*cyclo*hexene (31 g.) and stannic chloride (52 g.), the temperature being kept at 25—35°. After a further ¼ hour's stirring, the mixture was poured on ice (70 g.) and extracted with ether. The ethereal extract was washed with water and with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and distilled, giving crude *tert.*-butyl 2-chloro-2-methyl*cyclo*hexyl ketone (32 g., 62%), b. p. 133—160°, n_D^{23} 1·4753—1·4800. This product was recovered almost unchanged after 3·5 hours' refluxing with diethylaniline, but dehydrochlorination was effected by refluxing the chloro-ketone (22 g.) with potassium hydroxide (9 g.) in 80% aqueous ethanol (25 ml.) for 1·5 hr. After dilution with water, the product was isolated with ether and distilled, giving the ethylenic *ketone* (9 g.), b. p. 111—113°/13 mm., n_D^{20} 1·4711 (Found : C, 80·3; H, 11·3. $C_{12}H_{20}O$ requires C, 79·9; H, 11·2%). Ultraviolet light absorption in EtOH : infl. at 2900 Å (ε = 45); ε at 2100 and 2200 Å, 2100 and 1100 respectively, corresponding to an isolated, trialkylated ethylenic bond (Bladon, Henbest, and Woods, *J.*, 1952, 2737). Infrared absorption (liquid film) : $\nu_{max.}$ 1701 (unconjugated C=O stretching). The 2 : 4-*dinitrophenylhydrazone*, which was formed slowly during 24 hr., after chromatography on alumina and elution with benzene, crystallised from ethanol as light orange needles, m. p. 136—138°, $\lambda_{max.}$ 3710 Å (ε 23,500 in $CHCl_3$) (Found : C, 59·7; H, 6·8; N, 15·6. $C_{18}H_{24}O_4N_4$ requires C, 60·0; H, 6·7; N, 15·6%).

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Studies in Light Absorption. Part XIII. Steric Effects in* ortho-*Substituted Styryl and Related Derivatives.*

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The effects of *ortho*-substituents on the ultraviolet spectra of styrene, benzylideneacetone, and related derivatives of the type Ph·CH=CHX are analysed in terms of the principles outlined in Part XI.*

The discussion given in the two preceding papers of steric effects in ultraviolet spectra of conjugated aromatic and ethylenic ketones led to the conclusion, amongst others, that marked hindrance to planarity is caused by interference between the groups attached to the carbonyl function, rather than between such groups and the carbonyl function itself. Since valency angles at a doubly bonded carbon tend to be about the same (120°) whatever the other ligands, it might be expected that conjugated systems involving C=C in place of C=O groups might exhibit similar effects. That this is indeed the case is qualitatively apparent from the spectra of substituted styrenes, stilbenes, etc. (*inter al.*, Ley, *Ber.*, 1917, **50**, 243; 1918, **51**, 1808; 1923, **56**, 771; Ramart-Lucas and Hoch, *Bull. Soc. chim. France*, 1935, 327; 1938, 848; R. N. Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 1658; 1943, **65**, 1815, 1818; Rodebush and Feldmann, *ibid.*, 1946, **68**, 896; Murray and Gallaway, *ibid.*, 1948, **70**, 3867; Beale and Roe, *ibid.*, 1952, **74**, 2302; Braude, Jones, and Stern, *J.*, 1947, 1087; Bryant, Kennedy, and Tanner, *J.*, 1949, 2389; Bharucha and Weedon, *J.*, 1953, 1571), and the present paper is concerned with a semiquantitative evaluation of these phenomena in terms of the principles outlined in Part XI (*loc. cit.*).

Data concerning *o*-alkylated styrenes and styryl derivatives are summarised in Table 1. Most of the data have been taken from the literature, but those relating to 2-methyl- and 2 : 6-dimethyl-benzylideneacetone and their derivatives are new; the synthesis of these

Table 1. *Ultraviolet absorption of* o-*alkylated styrene derivatives* (*main banns only*).

X =	H	$CH=CH_2$	CHMe·OH	COMe	CMe=N·NH·CO·NH_2
Ph·CH=CHX $\lambda_{max.}$ (Å)	2440 [1]	2800 [2]	2510 [3]	2860 [5]	3050 [5]
ε	14,000	28,300	19,500	22,200	38,600
2-Me·C_6H_4·CH=CHX $\lambda_{max.}$ (Å)	2450 [1]	2810 [2]	2550 [3]	2900 [5]	3040 [5]
ε	12,600	25,000	16,000	17,000	32,500
$\varepsilon/\varepsilon_0$	0·78	0·83	0·74	0·71	0·84
θ	28	24	30	33	23
2 : 6-$Me_2C_6H_3$·CH=CHX $\lambda_{max.}$ (Å)	—	—	—	2910 [5]	2820 [5]
ε	—	—	—	10,500	23,300
$\varepsilon/\varepsilon_0$	—	—	—	0·40	0·60
θ	—	—	—	50	39
2 : 4 : 6-$Me_3C_6H_2$·CH=CHX $\lambda_{max.}$ (Å)	2450 [2]	—	2510 [4]	2930 [4]	—
ε	7000	—	7500	14,000	—
$\varepsilon/\varepsilon_0$	0·35	—	0·29	0·50	—
θ	54	—	57	44	—

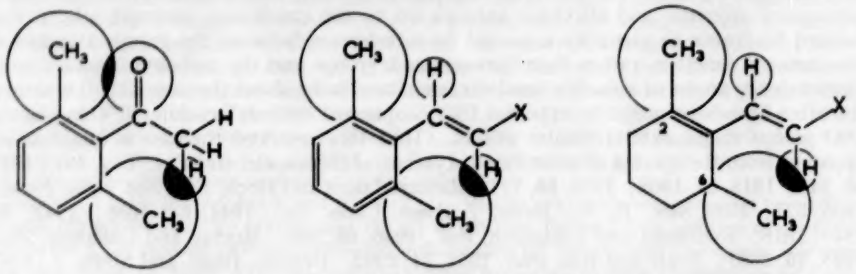
[1] Ramart-Lucas and Hoch, *loc. cit.* (in ethanol). The data to be found in the literature for styrene and substituted styrenes are extremely variable, probably owing to the presence of polymeric materials in some of the specimens used. The ε values cited are amongst the highest recorded. [2] Bryant *et al.*, *loc. cit.* (in octane). [3] Braude, Jones, and Stern, *loc. cit.* (in ethanol). [4] Bharucha and Weedon, *loc. cit.* (in ethanol). [5] This paper.

compounds is detailed in the Experimental section. It will be seen that *ortho*-methyl substituents without exception cause what have been labelled type (1) steric effects, *i.e.*, reductions in the intensities of the characteristic *K*-bands without accompanying hypsochromic wavelength displacements. Published data for styrenes, methylstyrylcarbinols, and phenylbutadienes (Bryant *et al.*, *loc. cit.*; Braude, Jones, and Stern, *loc. cit.*) show that *p*-methyl substituents generally cause a small increase in ε ($\Delta\varepsilon \sim +2000$) and it may be assumed that, in the absence of steric hindrance, *o*-methyl substituents would have similar effects. The ratios $\varepsilon/\varepsilon_0$ of the values of observed extinction coefficients to those expected

* Parts XI and XII, preceding papers.

on this basis in the systems Ph·CH=CHX vary appreciably with X but are of the order of 0·7—0·8 for one, and 0·3—0·5 for two *o*-methyl substituents. The interplanar angles θ between the phenyl and the CH=CHX group calculated from these ratios by the equation $\cos^2\theta = \varepsilon/\varepsilon_0$ (assuming $\theta = 0°$ for the unsubstituted compounds) range from *ca.* 20° to 30° for one, and from *ca.* 40° to 60° for two *o*-methyl substituents.

The values of θ in Table 1 are, not unexpectedly, similar to those for *o*-substituted acetophenones (Part XI, *loc. cit.*). All the compounds in this Table are known to possess, or may be assumed from their methods of preparation to possess, *trans*-configurations at the ethylenic double bond, and significant overlap will therefore occur only between an *o*-methyl substituent and the C=CH moiety (Fig. *b*). Such overlap will not differ very



greatly from that between an *o*-methyl substituent and the C–CH_3 moiety in acetophenones (Fig. *a*); C=CH is more rigid and the interfering hydrogen atom lies exactly in the plane of the chromophoric group, but this will be compensated to some extent by the fact that although none of the hydrogen atoms in C–CH_3 need lie in the plane of the chromophoric group, two hydrogen atoms instead of one will, then, by necessity, be within the repulsion radius of the *o*-methyl substituent.

Since the β-substituent X is not, according to the Figure, involved in steric hindrance to uniplanarity, the nature of the substituent should, as a first approximation, have no significant influence on θ. The second-order variation of θ with X which is actually observed may have several causes. One is that when X is itself a strongly conjugating group such as $CH=CH_2$, COMe, or CO_2H, it will affect the electronic forces which oppose non-planarity throughout the whole conjugated system. Another factor which has been neglected in the semiquantitative treatment given in this and the two preceding papers is that an accurate measure of transition probabilities is represented by integrated band areas rather than by $\varepsilon_{max.}$. The use of $\varepsilon_{max.}$ will cause little error as long as the band shapes in a series of spectra remain closly comparable, but may no longer be justified when the spectra show appreciable vibrational structure, as is the case with some of the triconjugated systems in Table 1.

It is of interest that, unlike 2 : 6-dimethylstyryl derivatives, 9-vinylanthracene derivatives show steric effects of type (2) and exhibit practically no conjugation between the anthryl group and the CH=CHX side chain (Braude, Fawcett, and Newman, *J.*, 1950, 793). Steric interference with the 1 : 8-hydrogen atoms of the anthryl groups is evidently much more severe than with the hydrogen atoms of *o*-methyl groups, presumably owing to the greater rigidity of the polycyclic system (cf. Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127; *Chem. Rev.*, 1947, **41**, 353).

We now turn to a comparison of styryl and diene derivatives. As in the case of aromatic and alicyclic ethylenic ketones (Part XII, *loc. cit.*), steric effects in the two series might be expected to be very similar. The only examples for which comparative data are available are the benzylideneacetones and the previously studied (Part VI, *J.*, 1949, 1890) alicyclic dienones of the ionone-type, and for these compounds the values of $\varepsilon/\varepsilon_0$ and θ are, in fact, in remarkably close agreement (Table 2).

It will be noted that the spectral properties of the 6 : 6-dimethyl*cyclo*hexene derivative, rather than the 2-methyl*cyclo*hexene derivative which shows hardly any steric hindrance, are comparable to those of 2-methylbenzylideneacetone. This is in agreement with the conclusion (Part VI, *loc. cit.*; cf. Braude, Bruun, Weedon, and Woods, *J.*, 1952, 1419;

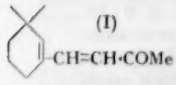
TABLE 2. *Comparison of steric effects in benzylideneacetones and alicyclic dienones* (R = CH=CH·COMe).

	$\lambda_{max.}$ (Å)	ε	$\varepsilon/\varepsilon_0$ *	θ *
	2860	22,000	1·0	0
	2230	11,000	—	—
	2910	17,000	0·71	33
	2220	10,000	—	—
	2810	11,000	0·40	50
	2910	10,500	—	—
	2810	20,800	1·0	0
	2280	4,100	—	—
	2810	13,000	—	—
	2900	13,500	0·65	36
	2230	6,500	—	—
	2960	10,700	0·46	47

* Based on long-wavelength bands.

MacGillavry, Kreuger, and Eichhorn, *Proc. k. ned. Akad. Wetenschap.*, 1951, **54**, *B*, 449) that the β-ionone and its analogues have *s-trans*-configurations (Fig. *c*), so that 6-methyl substituents cause much more interference than 2-methyl substituents. It is of interest that the parallelism between the phenyl and *cyclo*hexenyl derivatives extends, at least qualitatively, to the appearance, in the hindered compounds, of bands near 2230 Å probably associated with the partial "enone" [CH:CH·COMe] chromophores. The rather high intensities of these bands in the case of the substituted benzylideneacetones is probably due to overlap with short-wavelength absorption due to the benzene ring.

One apparent anomaly reported in the literature concerns 4-(3 : 3-dimethyl*cyclo*hex-1-enyl)but-3-en-2-one (I) for which Schinz and Seifert (*Helv. Chim. Acta*, 1951, **34**, 728) recorded $\lambda_{max.}$ 2850 Å (ε 12,500). Since the conjugated dienone system in (I) should not be subject to steric hindrance to planarity, the recorded ε value is surprisingly low. Through the kindness of Dr. Schinz, to whom we offer our cordial thanks for his co-operation, we have been able to redetermine the light absorption of a freshly purified sample of this ketone and of its 2 : 4-dinitrophenylhydrazone. The new values obtained for the ketone ($\lambda_{max.}$ 2800 Å, ε 25,000 in EtOH) and its derivative ($\lambda_{max.}$ 4000 Å, ε 35,000 in $CHCl_3$) are those expected for a normal, unhindered dienone.


(I)

EXPERIMENTAL

(For general methods, see Part XI, *loc. cit.*)

Benzylideneacetone (4-phenylbut-3-en-2-one), crystallised from pentane, had m. p. 42°, and gave a semicarbazone, m. p. 187—188°, and 2 : 4-dinitrophenylhydrazone, m. p. 226°.

2-Methylbenzylideneacetone (4-*o*-*Tolylbut-3-en-2-one*).—Aqueous sodium hydroxide (10%; 0·5 ml.) was added, with external cooling, to *o*-tolualdehyde (2·2 g.), acetone (5 ml.; "AnalaR"), and water (2 ml.). The mixture was shaken for 2 hr. at room temperature under nitrogen, and then acidified with dilute sulphuric acid and extracted with ether. Distillation of the ether extract afforded a mixture (1·9 g.) of aldol and unsaturated ketone, b. p. 89—110°/0·15 mm., n_D^{15} 1·5720—1·5550 (cf. Meerwein, *Annalen*, 1908, **358**, 89; Bharucha and Weedon, *J.*, 1953, 1571).

This product was heated with oxalic acid (4·0 g.) for 2 hr. on the steam-bath, under nitrogen. Water was added and the neutral products were isolated by extraction with ether, giving *o*-methylbenzylideneacetone, b. p. 84°/0·1 mm., n_D^{15} 1·5906. The *semicarbazone* crystallised from 2-methoxyethanol in hexagonal plates, m. p. 206—207° which became yellow in light (Found: C, 66·75; H, 7·0; N, 19·15. $C_{12}H_{15}ON_3$ requires C, 66·35; H, 6·95; N, 19·35%). The 2 : 4-*dinitrophenylhydrazone* crystallised from a large volume of ethyl acetate as dark red

prisms, m. p. 231° (Found : C, 60·5; H, 4·85; N, 16·6. $C_{17}H_{16}O_4N_4$ requires C, 60·0; H, 4·75; N, 16·45%).

2 : 6-*Dimethylbenzylideneacetone* [4-(2 : 6-*Xylyl*)*but*-3-*en*-2-*one*].—Condensation of 2 : 6-dimethylbenzaldehyde (1·4 g.) (Braude and Sondheimer, *J.*, 1955, 3754) and acetone (4 ml.), and dehydration of the product, as above, gave 2 : 6-*dimethylbenzylideneacetone* (0·6 g.), b. p. 94°/0·1 mm., n_D^{22} 1·5764 (Found : C, 83·0; H, 8·4. $C_{13}H_{14}O$ requires C, 82·75; H, 8·1%). The *semicarbazone* crystallised from aqueous methanol in plates, m. p. 171° (Found : C, 68·0; H, 7·5; N, 18·4. $C_{13}H_{17}ON_3$ requires C, 67·5; H, 7·4; N, 18·15%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in dark red prisms, m. p. 212—214° (Found : N, 16·2. $C_{18}H_{18}O_4N_4$ requires N, 15·8%).

When the initial period of shaking with sodium hydroxide was reduced to 2 hr., the yield of ketone was much lower, mainly unchanged aldehyde being recovered. A low yield of ketone was also obtained from a condensation in ethanol and sodium ethoxide (cf. Prelog, Führer, Hagenbach, and Frick, *Helv. Chim. Acta*, 1947, **30**, 113).

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Studies in Light Absorption. Part XIV. Steric Effects in* ortho-*Substituted Diphenyls.*

By E. A. Braude and W. F. Forbes.

[Reprint Order No. 6426.]

The effects of *ortho*-substitution and *ortho*-bridging on the ultraviolet spectra of diphenyl and diphenyl derivatives are discussed and compared with steric effects observed in the acetophenone and styrene systems (Parts XI and XIII).

ortho-Substituted diphenyls show steric effects of type (2), signifying non-planar ground and excited states. *ortho*-Bridged diphenyls such as 9 : 10-dihydrophenanthrene and dihydrodibenzoxepin, on the other hand, show predominantly steric effects of type (1), signifying non-planar ground states but near-planar excited states. It is suggested that the difference arises from the restriction on twist imposed by the 2- and 3-atom *ortho*-bridges. For the two examples mentioned, the mean interplanar angles in the ground state calculated by the equation $\cos^2\theta = \varepsilon/\varepsilon_0$ are *ca.* 20°, in good agreement with those indicated by models.

The introduction of *ortho*-substituents into short-bridged diphenyls increases the interplanar angle from about 20° to about 40°. In phenyldihydrothebaine, on the other hand, which contains a 5-membered *ortho*-bridge permitting a large twist, the interplanar angle deduced from the spectral data exceeds 60°.

The study of diphenyl and its derivatives has not only provided one of the cornerstones of what may now be termed " classical " stereochemistry, but also led to the recognition of the influence of steric conformation on the characteristic spectral properties of conjugated systems. The initial suggestion that the pronounced effect of *o*-substituents on ultraviolet-light absorption may be due to steric hindrance to uniplanarity appears to have been made by Kistiakowsky to explain the observations of Pickett, Walter, and France on dimesityl and hexachlorodiphenyl (*J. Amer. Chem. Soc.*, 1936, **58**, 2296) and further extensive investigations have been carried out in this field during the last fifteen years by Rodebush, R. N. Jones, E. E. Turner, and others [for a summary, see Braude and Waight, " Progress in Stereochemistry " (Ed. W. Klyne), Chapter 4, Butterworths, London, 1954].

* Part XI—XIII, preceding papers.

As a consequence, the diphenyl series represents the most fully documented example of the effects of *ortho*-substitution on the electronic spectra of a benzenoid system. Nevertheless, unanimity has not so far been reached even as to the detailed qualitative interpretation of many of the data and, indeed, the steric origin of some of the spectral phenomena has recently been questioned by Turner and his colleagues. The distinction between two different general types of steric effects and the semi-quantitative theory outlined in Part XI (*J.*, 1955, 3754) suggested a re-consideration of the evidence. This is the subject of the present paper.* In this connection, certain new data on mono-*o*-alkylated diphenyls are also reported.

ortho-*Substituted Diphenyls.*—Data for monosubstituted diphenyls are collected in Table 1. *o*-Alkyl substituents cause marked decreases in intensity as well as hypsochromic shifts, which are slightly larger with ethyl than with methyl, but do not differ appreciably for other primary and secondary alkyl groups. Similar decreases in ε are produced by *o*-hydroxyl and methoxyl substituents; in this case the observed hypsochromic shifts are quite small ($\Delta\lambda$ *ca.* −50 Å) but, when it is remembered that such groups normally produce bathochromic shifts of the same order in conjugated systems (cf. Bowden, Braude, and Jones, Part III, *J.*, 1946, 948; Bowden and Braude, Part X, *J.*, 1952, 1068), the "theoretical" hypsochromic shifts ($\Delta\lambda$ *ca.* −100 Å) are comparable with those observed with alkyl substituents. A strong hypsochromic shift is also observed in 2-iododiphenyl (Dunn and Iredale, *J.*, 1952, 1592); in this case the apparent effect on ε is small, but this is probably due to the overlap between absorption due to the diphenyl system and to the iodine atom in the 2200 Å region.

TABLE 1. *Ultraviolet light absorption of mono-o-substituted diphenyls.*

Ph_2 derivative	$\lambda_{max.}$ (Å)	ε *	Ph_2 derivative	$\lambda_{max.}$ (Å)	ε *
Unsubstituted [1–5]	2490	17,000	2-OH [3]	2450	8000
2-Me [1, 3, 4]	2350	10,500		2850	4500
2-Et [1]	2330	10,500	2-OMe [4, 3]	2450	11,000
2-Pr^n [1]	2330	10,000		2850	5000
2-Pr^i [1]	2330	11,000	2-I [5]	2290	17,000
2-Bu^s [1]	2330	10,500		2500	5000

* There are considerable variations between the values recorded by different workers, or even by the same workers [3, 4] on different occasions. The data in the Table are taken from the first reference cited.

[1] Present work (in ethanol). [2] Williamson and Rodebush, *J. Amer. Chem. Soc.*, 1941, **63**, 3018 (in ethanol). [3] Friedel, Orchin, and Reggel, *ibid.*, 1948, **70**, 199 (in *cyclo*hexane). [4] Friedel and Orchin, "Ultraviolet spectra of aromatic compounds," Wiley, New York, 1951 (in *cyclo*hexane). [5] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854 (in hexane). [6] Dunn and Iredale, *J.*, 1952, 1592 (in hexane).

TABLE 2. *Ultraviolet-light absorption of di-o-substituted diphenyls.*

Ph_2 derivative	Diphenyl band $\lambda_{max.}$ (Å)	Diphenyl band ε	Phenyl or phenoxy-band $\lambda_{max.}$ (Å)	Phenyl or phenoxy-band ε	Ph_2 derivative	Diphenyl band $\lambda_{max.}$ (Å)	Diphenyl band ε	Phenoxy-band $\lambda_{max.}$ (Å)	Phenoxy-band ε
Unsubstituted [1]	2490	17,000	—	—	2 : 2′-$(OMe)_2$ [4]	<2300	—	2770	6000
2 : 2′-Me_2 [2] ...	(2270) *	6,800	2635	800	3 : 3′-$(OMe)_2$ [4]	2500	12,000	2850	6000
3 : 3′-Me_2 [2] ...	2550	16,500	—	—	4 : 4′-$(OMe)_2$ [4]	2630	21,700	—	—
4 : 4′-Me_2 [2] ...	2600	20,000	—	—					
2 : 2′-$(OH)_2$ [3] ...	2420	10,000	2850	6000					
3 : 3′-$(OH)_2$ [3] ...	2550	12,000	2950	6000					
4 : 4′-$(OH)_2$ [3] ...	2650	22,400	—	—					

* Inflection.

[1] Present work (in ethanol). [2] Beaven, Hall, Lesslie, Turner, and Bird, *J.*, 1954, **131** (in ethanol). [3] Williamson and Rodebush, *loc. cit.* (in ethanol). [4] Williamson and Rodebush, *loc. cit.* (in hexane).

Data for disubstituted diphenyls are given in Table 2. It is apparent that the hypsochromic shifts produced by two *o*-methyl or *o*-methoxyl substituents are approximately twice as great as those due to one substituent, but the precise relations are rather blurred

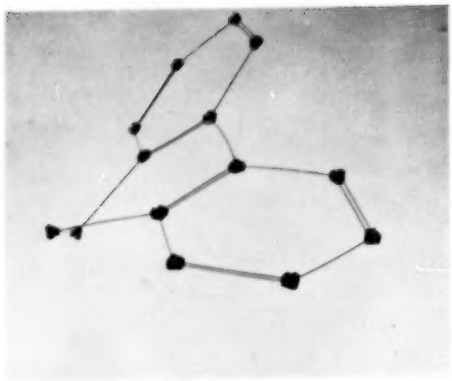
* For preliminary summaries, see Braude, *Chem. and Ind.*, 1951, 1002; *Experientia*, 1955, in the press; Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117).

by the fact that, particularly in di-*o*-tolyl, the displaced *K*-band overlaps with the short-wavelength absorption due to the separate phenyl rings (cf. Part X; Beaven *et al.*, *loc. cit.*). Although few data are available for mono-*m*- or -*p*-substituted diphenyls, those for *mm'*- and *pp'*-disubstituted derivatives show that in these positions, alkyl and methoxyl substituents exert normal variochromic effects of opposite sign, and it is therefore reasonable to regard the *ortho*-effects as steric in origin. (The effect of *m*-methoxyl groups on ε, which is somewhat exceptional, is discussed below.) Scale-projections employing double covalent radii, which represent a suitable measure of interference between non-bonded atoms (Part XI, *loc. cit.*), indicate appreciable overlap between an *ortho*-substituent such as Me or MeO and the *o'*-hydrogen atoms of the other phenyl ring in diphenyl. The fact that either one or two *ortho*-substituents, unless they are exceptionally large, do not confer measurable optical stability on the rotational enantiomorphs at room temperature (cf. Adams and Yuan, *Chem. Rev.*, **1933**, **12**, 261) shows that the energy barrier to uniplanarity does not exceed *ca.* **15** kcal./mole in the ground state, but this sets no definite limit to the hindrance in the excited state. The hypsochromic shift from 2500 to 2350 Å due to one *o*-methyl substituent actually corresponds to an increase in transition energy of 7 kcal./mole, which is the amount by which the energy level of the electronic excited state has been raised relative to that of the ground state and it is obviously reasonable that the effect of two such substituents should be about twice as great. The fact that there are only second-order differences between the effects of methyl, ethyl, and other primary alkyl groups is in agreement with the observations made in the acetophenone series (Part XI, *loc. cit.*); all but the methylene group attached directly to the phenyl ring can adopt conformations such that they cause little or no additional interference.

If the steric origin of the spectral displacements in mono-*o*-substituted diphenyl is accepted, this system provides an excellent example of what we have termed steric effects of type (2), *i.e.*, those involving hypsochromic wavelength shifts as well as changes in intensity. This contrasts with the position with *o*-substituted acetophenones and styrenes (Parts XI and XIII) which exhibit steric effects of type (1), *i.e.*, decreases in intensity without unusual changes in wavelength. A behaviour intermediate between these two has been observed in *o*-substituted phenylpyrimidines (Russell, *J.*, 1954, 2951). The divergence in spectral behaviour is at first sight surprising, since the geometries of the relevant parts of these systems and the areas of steric overlap are quite similar. There is, however, an important difference between the diphenyl system on the one hand, and the acetophenone and styrene systems on the other, which can be appreciated by considering, for example, 2-methyldiphenyl: the two possible uniplanar conformations of this compound are identical and involve the same extent of steric hindrance, whereas the two uniplanar conformations of 2-methylacetophenone or 2-methylstyrene are not identical and one involves much less steric hindrance than the other. Hence the steric hindrance produced by an *o*-methyl substituent will be effectively much larger in the diphenyl than in the other two systems, and the probability of any *o*-substituted diphenyl molecule's occupying a near-planar vibrational state will be extremely low. Thus, the conditions pre-requisite for the display of steric effects of type (1) no longer exist.

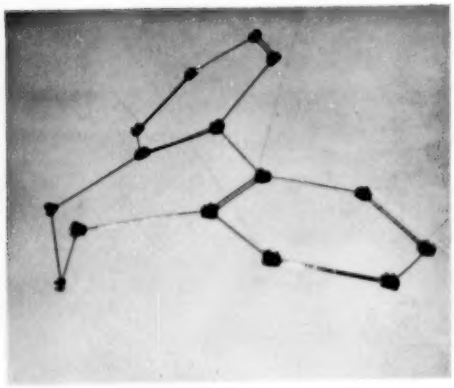
Secondly, the forces resisting in-plane bending will be considerably greater in the case of hydrogen atoms or methyl groups attached to a phenyl ring than when they are attached to a carbonyl or ethylenic group; this is reflected, for example, in the infrared C–H bending frequencies (cf. Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1954). A third factor, which is related to the second, is that owing to the, albeit slight, repulsion between *o*-hydrogen atoms, the equilibrium interplanar angle in diphenyl itself may deviate more from 0° than in styrene or acetophenone, so that any additional hindrance to other *ortho*-substituents will be more effective. An interplanar angle as high as 45° has been reported (Bastiansen, *Acta Chem. Scand.*, 1949, **3**, 408) for gaseous diphenyl, though the two rings appear to be coplanar in the solid, crystalline state (Dhar, *Indian J. Phys.*, 1932, **7**, **43**; *Proc. Nat. Inst. Sci. India*, 1949, **15**, 11); in solution the interplanar angle will presumably have an intermediate value. Unpublished calculations by Coulson and Longuet-Higgins indicate that the decrease in repulsion energy between the *o*-hydrogen atoms and the decrease in resonance energy resulting from non-planarity are practically

FIG. 1.



Scale model of 9 : 10-*dihydrophenanthrene.*

FIG. 2.

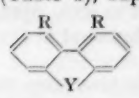


Scale model of 2 : 7-*dihydro*-3 : 4-5 : 6-*dibenzoxepin.*

(*To face p.* 3779.

balanced for interplanar angles of up to about 20°, so that there should be almost free rotation through an angle of this magnitude.* No electron-diffraction studies appear to have been carried out on styrene or acetophenone.

ortho-*Bridged Diphenyls.*—In fluorene (I; Y = CH_2, R = H), the two rings must be practically uniplanar in order to accommodate the methylene bridge. The fact that fluorene exhibits a " diphenyl-type " band slightly more intense than diphenyl itself (Table 3), supports the assumption that diphenyl is near-planar in solution; the small increase in ε is similar to that found in di-*p*-tolyl and may be ascribed to the normal substituent effect of the alkyl group, *i.e.*, fluorene shows the absorption of a planar, *oo'*-disubstituted diphenyl. In addition, fluorene has a band at longer wavelengths which has been ascribed to hyperconjugative interaction of the two rings through the methylene bridge (Part VIII, Braude, *J.*, 1949, 1902). Replacement of the CH_2 by a $CH_2{\cdot}CH_2$ bridge in 9 : 10-dihydrophenanthrene leads to a fall in ε of both bands. For the long-wavelength band, the decrease is to be expected, independently of steric effects, since hyperconjugative interaction will be diminished. For the " diphenyl-type " band, the decrease is to be expected since the ethane bridge will force the two benzene rings out of plane. Models show (Fig. 1) that, for the saturated carbon atoms to maintain their tetrahedral valency angle, the interplanar angle must be *ca.* 20° (cf. Beaven *et al.*, *loc. cit.*); this is in close agreement with the value of 18° obtained by applying the equation $\cos^2\theta = \varepsilon/\varepsilon_0$, assuming that ε_0 will be the same as for fluorene, *i.e.*, $\varepsilon/\varepsilon_0 = 17{,}000/19{,}000 = 0{\cdot}89$.



(I)

TABLE 3. *Ultraviolet-light absorption of* ortho-*bridged diphenyls.*

Compound *	Diphenyl band $\lambda_{max.}$ (Å)	ε	$\varepsilon/\varepsilon_0$ †	$\theta°$	Long-wavelength band $\lambda_{max.}$ (Å)	ε	Solvent
Fluorene [2]	2600	19,000	1·00	0	3000	10,000	E
9 : 10-Dihydrophenanthrene [1]	2640	17,000	0·90	18	2995	4,500	E
o : *o'*-Dimethyl derivative [3]	2600	16,000	0·84	24	—	—	E
o : *o'*-Dimethoxy-derivative [1]	2720	13,500	0·71	32	3045	9,300	E
2 : 7-Dihydrodibenzoxepin [1]	2500	16,500	0·87	21	—	—	H
o : *o'*-Dimethyl derivative [3]	2450	11,000	0·58	41	—	—	E
o : *o'*-Dimethoxy-derivative [1]	2530	8,700	0·46	47	2935	10,000	H
N-Acetylcolchinol methyl ether (II) [4]	2620	20,000	1·05	0	—	—	E
2 : 7-Dihydrodibenzazepinium bromide [1]	2480	15,000	0·79	27	2720	4,800	W
o : *o'*-Dimethoxy-derivative [1]	2375	11,500	0·61	39 ‡	2975	10,500	W
Phenyldihydrothebaine [5]	2810	5,600	0·29	57 §	—	—	?

* The designation *o* : *o'* refers to the positions of R in (I).

† The data refer variously to ethanol (E), hexane (H), or water (W) solutions. The comparisons are, nevertheless, justified, as measurements from one laboratory (ref. 1) show that ε is little solvent-dependent in this series.

‡ This value is probably too small, because it neglects the hypsochromic shift.

§ This value is a minimum, because any diphenyl absorption evidently overlaps with absorption due to the partial phenoxy-chromophores, and the latter has been neglected in calculating θ.

[1] Beaven *et al.*, *loc. cit.*, 1952. [2] Mayneord and Roe, *Proc. Roy. Soc.*, 1937, *A*, **158**, 634. [3] Wittig and Zimmermann, *Chem. Ber.*, 1953, **86**, 629. [4] Horowitz *et al.*, *ibid.*, 1950, **72**, 4331. [5] Small, Sargent, and Bralley, *J. Org. Chem.*, 1947, **12**, 839.

(The justification for equating ε_0 with the value for fluorene rather than that for diphenyl is that this makes an allowance for the normal, small increase in intensity due to the alkyl substituent; the importance of taking these effects into account has been demonstrated in other cases; cf. Part XI, *loc. cit.*)

The introduction of *o*-substituents into 9 : 10-dihydrophenanthrene (I; Y = $CH_2{\cdot}CH_2$, R = H) would be expected to increase further the angle between the benzene rings. The effects should be much less marked than in diphenyl, however, because they will be opposed by the ethane bridge and because the twist which already exists in 9 : 10-dihydrophenanthrene will facilitate the accommodation of *o*-substituents. In fact, the data for 9 : 10-dihydro-**4** : 5-dimethyl- and -**4** : 5-dimethoxy-phenanthrene (Table 3) show that, in contrast to diphenyl, *o*-substituents produce steric effects of type (1) (decrease in ε without hypsochromic shift) rather than of type (2). The " locking effect " of the ethane bridge

* We are indebted to Professor C. A. Coulson, F.R.S., for communicating and allowing us to quote these results, first presented by him at a Conference held in Washington in September, 1951.

is evidently sufficient to enforce a near-planar conformation of the two rings in the excited state; and the interplanar angles of about 30° calculated for the ground state are considerably *less* than those deduced for the correspondingly *o*-substituted acetophenones and styrenes (Part XI and XIII), in which rotation is not structurally restricted.

In addition to the decrease in ε of the diphenyl-type band, 9 : 10-dihydro-4 : 5-dimethoxyphenanthrene, but not the dimethyl derivative, shows an enhancement of the 3000 Å band. This enhancement ($\Delta\varepsilon = +6000$) may be ascribed to superposition of absorption due to the " phenoxy " chromophores $MeO{\cdot}C_6H_4-$ and is almost exactly equal to the difference in ε between, for example, diphenyl and 3 : 3'-dimethoxydiphenyl in this wavelength region.

One condition for the display of steric effects of type (I) is that steric hindrance to planarity should not exceed *ca.* 3 kcal./mole (Part XI). It is gratifying to note that the height of the energy pass between the ground state and the coplanar state of 9 : 10-dihydrophenanthrene has recently been estimated as 1·4 kcal./mole (Howlett, *J.*, 1955, 1249).

We next consider 2 : 7-dihydro-3 : 4-5 : 6-dibenzoxepin derivatives (I; Y = $CH_2{\cdot}O{\cdot}CH_2$). The parent compound again exhibits a typical diphenyl-type band, but the intensity is slightly lower than in dihydrophenanthrene and the calculated interplanar angle (21°) is slightly larger. As in the case of dihydrophenanthrene (see above) this angle is in excellent agreement with that indicated by scale models (see Fig. 2), the valency angle at the oxygen atom being taken as *ca.* 110° as in other ethers (cf. Lander and Svirbely, *J. Amer. Chem. Soc.*, 1945, **67**, 322; Everard and Sutton, *J.*, 1949, 2312).

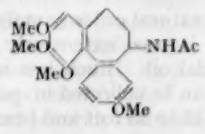
The introduction of two "*o*"-methoxy groups into dihydrodibenzoxepin again causes a decrease in ε of the " diphenyl-type " band and an increase in the interplanar angle to 47°. As in dimethoxydihydrophenanthrene, there is at the same time an increase in the absorption in the 3000 Å region, due to the two " phenoxy "-chromophores.

A different interpretation of the absorption of dihydrodibenzoxepin and its derivatives has been given by Turner, Beaven, and their colleagues (*loc. cit.*), to whom we owe many of the data just discussed, and, since this forms the central part of their theory of the spectral properties of substituted diphenyls, it will be considered in some detail. The starting point of their theory is the assumption, based on models of " Catalin " type (Beaven, personal communication; cf. Settatree, Thomas, and Yardley, *Nature*, 1950, **166**, 59) that the interplanar angle between the benzene rings in dihydrodibenzoxepin is " about 50°." Since the absorption of the oxepin is very similar to that of dihydrophenanthrene, Beaven *et al.* conclude that this " would suggest that in the oxepin the phenyl groups are no less conjugated and hence no less coplanar than in diphenyl. Since, however, the oxepin cannot be coplanar, it follows that the diphenyl-type spectrum does not provide sure evidence for a coplanar configuration." Further, they considered that since, in their view, the benzene rings in dihydrodibenzoxepin are already at an angle of *ca.* 50°, the introduction of "*o*"-methoxyl groups should have no steric consequences. These arguments require the decrease in ε brought about by *o*-methoxyl groups to be explained by other than steric effects, and Beaven *et al.* provide such an explanation by postulating that the weakening of the diphenyl-type band and the appearance of longer-wavelength absorption is due " primarily to mesomeric interaction between the methoxyl groups and the separate rings to which they are attached, with consequent reduction in the conjugation between the two rings." The fact that a smaller decrease in the ε of the diphenyl-type band is observed in 9 : 10-dihydro-4 : 5-dimethoxyphenanthrene is considered to be due to out-of-plane bending of the methoxyl group so that their mesomeric interaction and the reduction in conjugation between the two rings is less effective. This interpretation appears to neglect the fact that the intensity of long-wavelength absorption is almost exactly the same in 2 : 7-dihydro-4 : 5-dimethoxydibenzoxepin and 9 : 10-dihydro-4 : 5-dimethoxyphenanthrene. Moreover, the assumption of an angle of 50° between the phenyl rings in dihydrodibenzoxepin is questionable, and is not supported by " open " scale models, such as those shown in Fig. 2. The main difficulty with Turner's theory, however, appears to us to be that it does not account for the effects of *o*-methyl substituents. Methyl groups are known to have much weaker mesomeric effects than methoxyl groups and produce no marked long-wavelength absorption when attached to benzene rings; yet the data in Table 3 clearly show that they

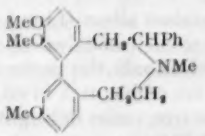
cause comparable reductions in the intensities of the diphenyl type bands in di-*o*-tolyl as well as in 9 : 10-dihydro-4 : 5-dimethylphenanthrene. These reductions can hardly be ascribed to electronic interactions between the methyl substituents and the separate benzene rings.

The effects of *o*-substituents on diphenyl-type absorption thus seem more plausibly explained as mainly due to steric rather than electronic interactions, and in a more recent paper, Hall, Ridgwell, and Turner (*J.*, 1954, 2498) appear to have accepted our theory of transitions between non-planar ground and near-planar excited states as providing an adequate interpretation of the spectral data of 1-phenylnaphthalene-2′-carboxylic acid derivatives. It still remains, however, to account for the above-mentioned effect of *m*-methoxyl substituents, which though smaller than those of *o*-substituents, are appreciable. Beaven *et al.* have interpreted these effects as mesomeric interactions similar to those involved in the case of *ortho*-substituents. An alternative view is that *meta*-substituents exert indirect steric effects by " buttressing " the *o*-hydrogen atoms against in-plane bending away from the diphenyl link. Convincing evidence for the existence of the " buttressing effect " has been provided by measurements on the ease of racemisation of *ortho*- and *meta*-substituted, optically active diphenyls (Chien and Adams, *J. Amer. Chem. Soc.*, 1934, **56**, 1787; Rieger and Westheimer, *ibid.*, 1950, **72**, 19). The effect is not sufficient to impart optical stability to diphenyls containing no *ortho*-substituents, but, as was previously pointed out (Part XI), electronic spectra are a much more sensitive index of steric effects than is optical resolvability. No steric effects are observed in mono-*meta*-substituted acetophenones or styrenes (Part XI and XIII, *loc. cit.*) because the parent systems are " comfortably " planar and the effect of a single substituent will, in any case, be small. In the diphenyl system, on the other hand, there is slight interference even between the *o*-hydrogen atoms in the parent compound, which are therefore much more susceptible to the buttressing effect.

The remaining *oo*′-bridged diphenyls in Table 3 may now be briefly considered. A three-carbon bridge, as in *N*-acetylcolchinol methyl ether (II), evidently causes no significant deviation to planarity, as has already been pointed out by Horning, Ullyot, and their co-workers (*J. Amer. Chem. Soc.*, 1950, **72**, 4331; cf. Rapoport, Allen, and Cisney, *ibid.*, 1955, **77**, 670). The dihydrodibenzazepinium bromide (as I; Y = $CH_2 \cdot \overset{+}{N}Ph \cdot CH_2$), like the other



(II)



(III)

unsubstituted compounds, also shows a relatively small reduction in diphenyl absorption, from which an interplanar angle of 27°, in good agreement with that indicated by models, can be deduced. In this case, however, *o*-methoxyl substituents cause not only a further reduction in intensity of the diphenyl-band, but also a hypsochromic shift, similar to that found in 2 : 2′-dimethoxydiphenyl. It appears that the dihydrodibenzazepinium system is sufficiently flexible for the *o*-methoxyl substituents to cause appreciable non-planarity in the excited as well as in the ground state, thus resulting in steric effects of type (2).

In contrast to dihydrodibenzazepinium bromide, the arsenic analogue (as I; Y = $CH_2 \cdot \overset{+}{As}Ph \cdot CH_2$) exhibits no diphenyl-type band (Beeby, Mann, and Turner, *J.*, 1950, 1923), indicating that the large arsenic atom does not allow the two phenyl rings to approach a near-planar arrangement even at the expense of some valency-angle distortion. This is confirmed by scale models which show that the phenyl rings are almost at right angles to one another. On the other hand, some interaction between the phenyl rings appears to exist in the lower homologues (as I; Y = $\overset{+}{As}Ph$ and $\overset{+}{Sb}Ph$) (Campbell and Poller, *Chem. and Ind.*, 1953, 1126) but detailed interpretation of these data is difficult because of superposition between diphenyl-type absorption and absorption due to the Ph–As chromophore (cf. Bowden and Braude, Part X, *J.*, 1952, 1068).

Lastly, phenyldihydrothebaine (III) provides an example of a diphenyl containing a five membered *oo'*-bridge, as well as one *o*-hydroxyl substituent. Unlike a two- or three-membered bridge, a five-membered bridge, by itself, will tend to rotate the one phenyl ring by an appreciable angle with respect to the other, and can readily accommodate the additional repulsion caused by an *ortho*-substituent. As was pointed out by Robinson in his notable derivation of the structure of phenyldihydrothebaine (*Nature*, **1947**, **60**, 815; *Proc. Roy. Soc.*, **1947**, *B*, **135**, 14; Bentley and Robinson, *J.*, 1952, 947), the non-planarity of the diphenyl system in this compound is apparent both from its optical resolvability and from its ultraviolet absorption; the spectral data indicate that the interplanar angle is at least about 60°, and probably even larger (Table 3).

Experimental.—We are indebted to Drs. Goodman and Wise (cf. *J. Amer. Chem. Soc.*, **1950**, **72**, 3076) for kindly providing the *o*-alkyldiphenyls.

After fractionation, 2-methyldiphenyl had b. p. 47°/0·03 mm., n_D^{21} 1·5908; 2-ethyldiphenyl had b. p. 57°/0·04 mm., n_D^{20} 1·5783; 2-*n*-propyldiphenyl had b. p. 68°/0·04 mm., n_D^{20} 1·5692; 2-*n*-butyldiphenyl had b. p. 62°/0·03 mm., n_D^{21} 1·5598; 2-*iso*propyldiphenyl had b. p. 65°/0·02 mm., n_D^{21} 1·5695. The spectra were determined on Hilger–Spekker and Beckman instruments. Some of the data are not in good agreement with those recorded in the American Petroleum Institute Collection (Nos. **94**, **202**, **248**, **284**, **285**, and **286**).

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Fatty Acids. Part III. The Constitution and Properties of Santalbic Acid.*

By F. D. Gunstone and W. C. Russell.

[Reprint Order No. 6485.]

Santalbic acid, the chief component acid in *Santalum album* (Linn.) seed oil, is shown to be *trans*-octadec-11-en-9-ynoic acid † and thus identical with ximenynic acid. Some reactions of this acid are reported.

The evergreen tree *Santalum album* (Linn.) of the natural order Santalaceae is well known for its highly scented wood (sandalwood) which is used extensively throughout India. Distillation of the wood affords the perfume sandal oil. Much less is known about the seeds except that they are edible, rich in oil, and can be collected in quantity from sandalwood plantations. The tree varies in height from 12 to 35 feet and bears fruit twice a year (Iyer, *Analyst*, **1935**, **60**, 319).

Previous investigators (Sreenivasaya and Narayana, Proc. 15th Indian Sci. Congr., 1928, p. 160; *J. Indian Inst. Sci.*, **1936**, **19**, *A*, 1; Iyer, *loc. cit.*; Rao, *J. Annamalai Univ.*, **1937**, **6**, 198; Kotasthane and Narayana, *Poona Agr. Coll. Mag.*, **1938**, **29**, 126) have shown that these seeds contain an oil (50—60%) which readily polymerises. The characteristics of the oil recorded by these workers show considerable variation; the iodine value lies between 100 and 150, the saponification value between 172 and 197, and the acetyl value between 20 and 40. There is evidence of something unusual in Kotasthane and Narayana's report that " solid " and " liquid " acids have a similar high iodine value.

Madhuranath and Manjunath, in a fuller investigation (*J. Indian Chem. Soc.*, 1938, **15**, 389), reported the presence in quantity of a solid octadecatrienoic acid (santalbic acid) which appears to be non-conjugated. This view was based on the observations that stearic acid resulted from hydrogenation in which three mols. of hydrogen are absorbed, that the acid failed to react with maleic anhydride, and that it differed from punicic acid, a stereoisomer of elæostearic acid. Since among naturally occurring octadecatrienoic acids the non-conjugated isomers are liquid and the conjugated isomers are solid we reinvestigated this problem.

* Part II, *J.*, 1954, 1611.

† Geneva numbering, CO_2H = 1.

Constitution of Santalbic Acid.—The ultraviolet spectrum of santalbic acid showed a maximum at 229 mμ (log ε 4·22) and an inflexion at 240 mμ (log ε 4·06). These values indicated immediately that the acid contains, not a conjugated triene as chromophore, but a diene or enyne system. A naturally occurring enyne acid, ximenynic acid, has been described (Ligthelm, Schwarz, and von Holdt, *J.*, 1952, 1088; Ahlers and Ligthelm, *J.*, 1952, 5039) and a comparison of the two acids and their *p*-bromophenacyl esters revealed their close similarity. Other enynes with similar ultraviolet spectra have been reported

	M. p.	Ultraviolet absorption	*p*-Bromophenacyl ester (m. p.)
Ximenynic acid ...	39—40°	229 mμ (log ε 4·21), 240 mμ (infl.)	53·8—54·2°
Santalbic acid [a]	38·5—39·5	229 mμ (log ε 4·22), 240 mμ (infl.)	53—54
Santalbic acid [b] ...	38·5—39	229 mμ (log ε 4·20), 240 mμ (infl.)	53·5—54

[a] Present work. [b] Hatt and Szumer, *Chem. and Ind.*, 1954, 962 (this work will be referred to below).

(Heilbron, Jones, and Weedon, *J.*, 1944, 140 and other references quoted there) and it is known that the corresponding dienes differ chiefly in their larger values of ε. The identity of santalbic and ximenynic acid has now been amply confirmed by hydrogenation, oxidation, infrared spectrum, and by comparison with a synthetic specimen (Grigor, McInnes, and McLean, *J.*, 1955, 1069).

Santalbic acid quickly absorbed hydrogen (three mols.) and gave stearic acid; oxidation with potassium permanganate in acetic acid solution gave heptanoic and azelaic acid; and the infrared spectrum was identical with that of synthetic ximenynic acid and contained, in particular, a band at 953 cm.$^{-1}$ indicative of a *trans*-ethylenic bond in conjugation with an acetylenic linkage.

This evidence indicated unsaturated centres in the 9 : 10- and the 11 : 12-position, one of which must be acetylenic since the compound required three mols. of hydrogen for saturation and no other unsaturated centre is present. The infrared absorption at 953 cm.$^{-1}$ further confirms the absence of a *trans-trans-* (988 cm.$^{-1}$) or *cis-trans-* (984 and 950 cm.$^{-1}$) diene (Ahlers, Brett, and McTaggart, *J. Appl. Chem.*, 1953, **3**, 433). There are thus only two possible structures for santalbic acid, (I) or (II), of which (I) has been assigned to

(I) $CH_3 \cdot [CH_2]_5 \cdot CH{:}CH \cdot C{\equiv}C \cdot [CH_2]_7 \cdot CO_2H$ $\quad$ $CH_3 \cdot [CH_2]_5 \cdot C{\equiv}C \cdot CH{:}CH \cdot [CH_2]_7 \cdot CO_2H$ (II)

ximenynic on the basis of ozonolysis to heptanal and azelaic acid (Ligthelm, Schwarz, and von Holdt; Hatt and Szumer, *locc. cit*) and confirmed by synthesis (Grigor, McInnes, and McLean, *loc. cit.*). Before this synthetic work we had independently shown that santalbic acid has structure (I) by a method which provides additional proof of the *trans*-configuration of the double bond.

It is known that peracids react much more readily with ethylenic than with acetylenic bonds (Raphael, " Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955, p. 33) and we have applied Swern's performic acid oxidation procedure to santalbic acid (Swern, Billen, Findley, and Scanlan, *J. Amer. Chem. Soc.*, 1945, **67**, 1786). A dihydroxy-acid was isolated, though in poorer yield than usual for this reaction. The product readily took up two mols. of hydrogen to give an acid (m. p. 127—128°) shown to be 11 : 12-dihydroxystearic acid by its oxidation to heptanal and 10-formyldecanoic acid with periodate and to heptanoic and 1 : 11-undecanedioic acid with potassium permanganate. Comparison of the melting point with that of the known *threo-* (m. p. 94°) and *erythro*-11 : 12-dihydroxystearic acids (m. p. 129°) (Bounds, Linstead, and Weedon, *J.*, 1954, 4219) clearly shows our product to be the *erythro*-isomer and since hydroxylation by performic acid is equivalent to *trans*-addition the double bond must have had the *trans*-configuration. Santalbic acid is therefore octadec-*trans*-11-en-9-ynoic acid (I) and identical with ximenynic acid. Dr. McLean has reported that samples of santalbic acid, its *p*-bromophenacyl ester, and 11 : 12-dihydroxystearolic acid supplied by us showed no depression of melting point when mixed with their synthetic products.

Periodate oxidation of dihydroxystearolic acid gave heptanal and a product considered to be 10-formyldec-9-ynoic acid. Though not very stable this compound was satisfactorily analysed, its ultraviolet absorption measured, and a 2 : 4-dinitrophenylhydrazone prepared.

This last, isolated pure only with difficulty, was yellow though ethylenic αβ-unsaturated carbonyl compounds usually give orange or red dinitrophenylhydrazones [the dinitrophenylhydrazone of 11-formylundec-10-enoic acid is deep orange (Part II) but Lunt and Sondheimer (*J.*, **1950**, **3361**) report a yellow 2 : 4-dinitrophenylhydrazone for but-2-ynal and hept-2-ynal]. This decreased intensity of colour is probably due to the fact that the π electrons of a triple bond are more tightly bound than those of a similarly situated double bond (Raphael, *op. cit.*, p. 208). The ultraviolet spectrum of the acetylenic aldehyde is interesting in that a more intense absorption was observed for hexane solutions than for ethanol solutions; and, in addition, other maxima were noted in the former solvent which previously have not been reported. The lower absorption in alcohol may be due to hemiacetal formation, as suggested by Ashdown and Kletz (*J.*, 1948 1454; cf. Crombie, *J.*, 1955, 1011). The values obtained in this work and those obtained for similar compounds by other investigators are summarised in the Table.

Aldehyde	$\lambda_{max.}$ (mμ)	ε EtOH	ε *n*-Hexane	Aldehyde	$\lambda_{max.}$ (mμ)	ε EtOH	ε *n*-Hexane
$CH_3{\cdot}C{\equiv}C{\cdot}CHO$ [a]	225	2800	—	$HO_2C{\cdot}[CH_2]_7{\cdot}C{\equiv}C{\cdot}CHO$	208	—	7800
$CH_3[CH_2]_5{\cdot}C{\equiv}C{\cdot}CHO$ [a]	227	3200	—		222	—	6500
$CH_3{\cdot}[CH_2]_4{\cdot}C{\equiv}C{\cdot}CHO$ [b]	227	—	8000		231	4000	6000

[a] Lunt and Sondheimer, *loc. cit.* [b] Crombie, *loc. cit.*

Catalytic Reduction of Santalbic Acid.—Ligthelm *et al.* (*loc. cit.*) failed to convert the enynoic into the corresponding dienoic acid, but, using the poisoned catalyst of Lindlar (*Helv. Chim. Acta*, 1952, **35**, 446), we have now succeeded in preparing octadeca-*cis*-9-*trans*-11-dienoic acid. In ethanol solution there was no break in hydrogen absorption and the reaction was stopped after the required amount of hydrogen had been absorbed; in light petroleum solution there appeared to be no reduction. Our product is similar to that obtained from linoleic acid by alkali-isomerisation (Nichols, Herb, and Riemenschneider, *J. Amer. Chem. Soc.*, 1951, **73**, 247). In the presence of iodine it readily isomerised to the familar *trans-trans*-dienoic acid (Mangold, *Monatsh.*, 1894, **15**, 309), characterised as its maleic anhydride adduct. It is interesting to compare the ultraviolet spectra of the enynoic and of the two dienoic acids. The *trans-cis*-diene was not purified and the inflexion at 240 mμ may be due to traces of santalbic acid; this is less likely in the *trans-*

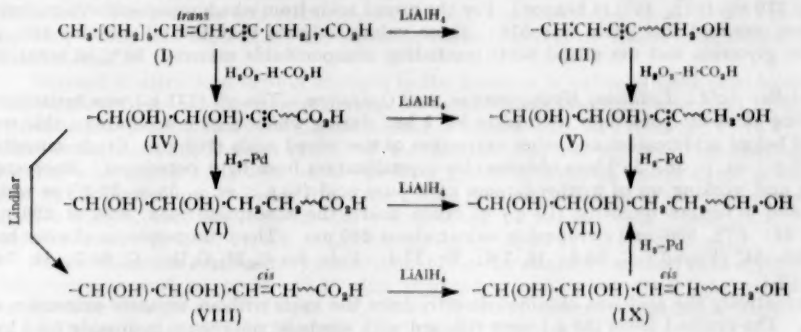
	$\lambda_{max.}$ (ε)	Inflexion
trans-11-en-9-yn-	229 mμ (16,600)	240 mμ
trans-11-*cis*-9-dien-	231 mμ (24,000)	240 mμ
trans-11-*trans*-9-dien-	231 mμ (33,300)	227, 239 mμ

trans-diene which shows inflexions on both sides of the maximum. The maxima agree well with these previously reported (Nichols *et al.*, *loc. cit.*; Kass, "Protective and Decorative Coatings," ed. Mattiello, J. Wiley & Sons, 1944, Vol. IV, p. 362; van der Hulst, *Rec. Trav. chim.*, 1935, **54**, 639, 644).

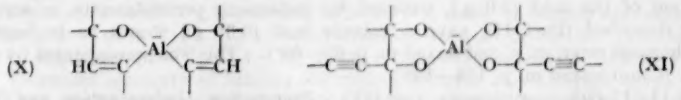
Lithium Aluminium Hydride Reduction of Santalbic Acid and its Derivatives.—Reduction of santalbic acid affords the corresponding alcohol (III) as reported by Ligthelm, von Rudloff, and Sutton (*J.*, 1950, 3187). Acetylenic bonds are unaffected by lithium aluminium hydride except when connected to a carbon atom carrying a hydroxyl group; they are then stereospecifically reduced to *trans*-ethylenic bonds (Raphael, *op. cit.*, p. 30 and references there cited). By this reaction it was hoped to convert dihydroxystearolic acid into 1 : 11 : 12-trihydroxyoctadec-*trans*-9-ene but despite several attempts only the acetylenic triol (V) was obtained. This also resulted from per-acid oxidation of the enyne alcohol (III). Dihydroxyoleic acid (VIII) however was produced from dihydroxystearolic acid by catalytic reduction (Lindlar) and this, with lithium aluminium hydride, afforded the *cis*-ethylenic triol (IX). The saturated triol (VII) was obtained by lithium aluminium hydride reduction of dihydroxystearic acid (VI) or by catalytic reduction of either the acetylenic triol (V) or the *cis*-ethylenic triol (IX).

Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker (*J.*, 1952, 1101) have suggested that stereospecific reduction of an α-hydroxy-acetylenic compound by

lithium aluminium hydride involves formation of an intermediate aluminium complex of type (X), and the only reported failure of this reaction has been attributed to steric hindrance (Raphael, *op. cit.*). This is unlikely in the present case and we suggest that the



glycol preferentially forms a complex of type (XI) in which the triple bond is not involved and hence not reduced. This constitutes a limitation of this reaction in that it is not applicable to acetylenic glycols of the type –C(OH)·C(OH)·C:C–. Glycols of the type –C(OH)·C:C·C(OH)– have been reduced (unpublished results of the Manchester school quoted by Raphael, *op. cit.*, p. 114) but in this case a complex of type (XI) involving four hydroxyl groups is unlikely on spatial grounds.



Santalum album *Seed Oil.*—Spectroscopic data show that the mixed acids (excluding unsaponifiable material) contain 95% of santalbic acid along with 5% of other unidentified acids. The enynoic acid has now been recognised by Ligthelm, Horn, Schwartz, and von Holdt (*J. Sci. Food Agric.*, 1954, **5**, 281) in three South African *Ximenia* species (N. O. Olacaceae) [*X. caffra* (24·3%), *X. caffra* var. *natalensis* (22·0%), *X. americana* var. *microphylla* (21·9%)], and by Hatt and Szumer (*Chem. and Ind.*, 1954, 962) in two species of the *Santalum* genus (N. O. Santalaceae) [*S. acuminatus* (D.C.) (the sweet Quandong) and *S. Murrayana* (F. v. M) (the Bitter Quandong) (40—43%)], in addition to the present source (88%). These two genera belong to closely related families grouped in the Santalales and apart from two analyses (Puntambekar and Krishna, *J. Indian Chem. Soc.*, 1937, **14**, 268; Boekenoogen *Fette u. Seifen*, 1939, **46**, 717) of *X. Americana* seed oil which may be in error (cf. Ligthelm, Horn, Schwarz, and von Holdt, *loc. cit.*) each species of these two genera yet examined contains this enynoic acid.

Ligthelm (*Chem. and Ind.*, 1954, 249) has reported that in *X. caffra* seed oil the enynoic acid is accompanied by a small amount of hydroxy-acid, probably 8-hydroxyoctadec-11-en-9-ynoic acid, but we have found no evidence of such an acid in sandal wood oil.

It is apparent from the figures quoted that sandal seeds provide the best source of this enynoic acid which is readily isolated in high yield by crystallisation of the mixed acids. Starting with the less satisfactory sources the South African and Australian workers have had to use distillation, chromatography, or urea complex formation before crystallisation and have isolated the acid in much lower yield.

Experimental

Absorption spectra were determined with a Unicam quartz spectrophotometer, ethanol being the solvent except where otherwise stated. Light petroleum refers to the fraction of b. p. 40—60°.

S. album *Seed Oil.*—The dried seeds were spherical, about ¼" in diameter, and brown, and had an average weight of 0·15 g. When coarsely ground in a mortar and extracted with light petroleum the oil (53·5%) was obtained as a viscous, pale greenish-yellow liquid of iodine value 152·5, sap. equiv. 332·8, containing 6·9% of unsaponifiable material, and having absorption max. at 229 mμ ($E^{1\%}_{1\,cm.}$ 497) in hexane. For the mixed acids from which unsaponifiable material had been removed this value was 570. These values indicate that the oil contains 88% of santalbic glyceride and the mixed acids (excluding unsaponifiable material) 95% of santalbic acid.

Santalbic Acid : Isolation, Hydrogenation, and Oxidation.—The oil (131 g.) was hydrolysed by boiling alcoholic potassium hydroxide for 1 hr., during which a gum separated; this was rejected before acidification and ether extraction of the mixed acids (103 g.). Crude santalbic acid (77 g.; m. p. 36—38°) was obtained by crystallisation from light petroleum. Recrystallisation and working up of mother-liquors gave pure acid (68 g.; m. p. 38·5—39·5°) as white plates and a further quantity (10 g.) of crude acid; the absorption max. was at 229 mμ (log ε 4·22; $E^{1\%}_{1\,cm.}$ 596) and an inflexion was at about 240 mμ. The *p*-bromophenacyl ester had m. p. 53—54° (Found : C, 65·6; H, 7·6; Br, 17·1. Calc. for $C_{34}H_{55}O_3Br$: C, 65·7; H, 7·4; Br, 16·8%).

Alternatively the acid was obtained directly from the seeds without separate extraction of the oil. The crushed seeds (30 g.) were refluxed with alcoholic potassium hydroxide for 1 hr., the solution filtered, and the filtrate diluted with water, acidified, and extracted (ether). The product (10·6 g.) gave santalbic acid (5·8 g.; m. p. 37—39°) when crystallised from light petroleum. Troublesome emulsions were encountered in the extraction.

Santalbic acid (0·5 g.), hydrogenated in the presence of palladium-charcoal, took up hydrogen equiv. to 3·0 mols. The product (0·53 g.) afforded stearic acid on crystallisation (m. p. 69—70°) (*p*-bromophenacyl ester, m. p. 90°) (both m. p.s were unchanged on admixture with authentic samples).

A portion of the acid (2·0 g.), oxidised by potassium permanganate in acetic acid as previously described (Part II), gave a volatile acid (0·36 g.) shown to be heptanoic acid (*p*-bromophenacyl ester, m. p. and mixed m. p. 68—69°). This was accompanied by azelaic acid (0·8 g.), m. p. and mixed m. p. 104—105°.

erythro-11 : 12-*Dihydroxystearolic Acid* (IV) : *Preparation, Hydrogenation, and Oxidation.*—Hydrogen peroxide (30%; 12 ml.) was added to a solution of santalbic acid (22 g.) in formic acid (98—100%; 240 ml.), and the mixture kept at 40° with stirring for 2½ hr. The product after recovery in the usual way (Swern *et al.*, *loc. cit.*) was crystallised from ether–light petroleum (1 : 1; 200 ml.). The crude dihydroxystearolic acid (8·4 g.) was purified by crystallisation from ethyl acetate and from alcohol, with charcoal if necessary. The pure acid (4·8 g.) melted at 88—89° (Grigor *et al.*, *loc. cit.*, give 89—90°) (Found : C, 69·5; H, 10·2. Calc. for $C_{18}H_{32}O_4$: C, 69·2; H, 10·3%).

Dihydroxystearolic acid (2·0 g.) when reduced (Pd–C; H_2 equiv. to 2·0 mols.) gave *erythro*-11 : 12-dihydroxystearic acid, m. p. 127—128° (from ethanol) (lit., 129°; Bounds, Linstead, and Weedon, *loc. cit.*) depressed on admixture with *erythro*-9 : 10-dihydroxystearic acid (m. p. 129—131°) (Found : C, 68·3; H, 11·1. Calc. for $C_{18}H_{36}O_4$: C, 68·3; H, 11·5%). Oxidised with potassium permanganate in acetic acid solution (see Part II), this acid (0·6 g.) gave heptanoic acid (0·15 g.) (*p*-bromophenacyl ester, m. p. and mixed m. p. 68—70°) and 1 : 11-undecanedioic acid (0·3 g.), m. p. 108·5—109·5° (identical with a specimen described below). Periodate oxidation of the dihydroxystearic acid (2·0 g.) (see Part II) afforded heptaldehyde which was identified as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 103—104° (Found : C, 53·3; H, 5·9. Calc. for $C_{13}H_{18}O_4N_4$: C, 53·0; H, 6·2%). This was accompanied by 10 *formyldecanoic acid*, m. p. 47—48° [from light petroleum (b. p. 60—80°)] (Found : C, 65·7; H, 9·9. $C_{11}H_{20}O_3$ requires C, 65·9; H, 10·1%), oxidised to 1 : 11-undecanedioic acid, m. p. 109—110° (lit., 110°) (Found : C, 60·9; H, 9·6. Calc. for $C_{11}H_{20}O_4$: C, 61·1; H, 9·3%). The 2 : 4-*dinitrophenylhydrazone* of ethyl 10-formyldecanoate resulted from an attempt to prepare the derivative of the acid in ethanol solution, and had m. p. 59—60° (Found : C, 55·7; H, 6·7; N, 13·9. $C_{19}H_{28}O_6N_4$ requires C, 55·9; H, 6·9; N, 13·7%).

Periodate oxidation of dihydroxystearolic acid (2 g.) gave heptanal (0·5 g.), characterised as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 105—105·5° (Found : C, 53·2; H, 6·0; N, 18·8. Calc. for $C_{13}H_{18}O_4N_4$: C, 53·0; H, 6·2; N, 19·0%), and as the semicarbazone, m. p. and mixed m. p. 108—108·5°. The non-volatile fission product was 10-*formyldec*-9-*ynoic acid*, m. p. 25·5—26·5° (Found : 67·3; H, 7·9. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%), absorption max. see p. 3784. The 2 : 4-*dinitrophenylhydrazone* prepared in acetic acid solution and purified

by passage through a column of silica gel was obtained as a deep yellow powder, m. p. 105·5—106·5° (Found : C, 53·9; H, 5·3; N, 14·7. $C_{17}H_{20}O_6N_4$ requires C, 54·2; H, 5·4; N, 14·9%).

Reductions with Lindlar's Catalyst.—Santalbic acid (2 g.) in ethanol (30 ml.) containing Lindlar's catalyst (200 mg.) and quinoline (80 mg.) was shaken with hydrogen which was steadily absorbed. The reaction was stopped after 200 ml. had been taken up (175 ml., 2 mol.). The product which was solid at 0° but liquid at room temperature was octadeca-*cis*-9 : *trans*-11-dienoic acid.

Exposed to ultraviolet light or sunlight in the presence of iodine in light petroleum solution this *cis-trans*-diene was isomerised to octadeca *trans*-9-*trans*-11-dienoic acid (1 g.), m. p. 48—50° which after crystallisation from alcohol melted at 53—54° (lit., 54°) (Found : C, 76·9; H, 11·5; Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%). For absorption max. see p. 3784. This *trans-trans*-diene reacted with maleic anhydride at 75° to form the diene addition product, m. p. 92·5—93·5 [lit., 88° (Böeseken and Hoevers, *Rec. Trav. chim.*, 1930, **49**, 1165), 94·5° (Kaufmann and Baltes, *Fette u. Seifen*, 1936, **43**, 93), 78—96° (Schmid and Lehmann, *Helv. Chim. Acta*, 1950, **33**, 1494)] (Found : C, 69·8; H, 8·8. Calc. for $C_{22}H_{34}O_5$: C, 69·8; H, 9·1%).

Partial reduction of dihydroxystearolic acid (1 g.) by the same method gave erythro-10 : 11-*dihydroxyoleic acid*, m. p. 68—68·5° after repeated crystallisation from light petroleum and finally from nitromethane (Found : C, 68·6; H, 10·8; microhydrogenation shows 1·1 C:C. $C_{18}H_{34}O_4$ requires C, 68·7; H, 10·9%; 1·0 C:C).

Reductions with Lithium Aluminium Hydride.—A solution of santalbic acid (1·6 g.) in dry ether (25 ml.) was slowly added to a suspension of lithium aluminium hydride (0·3 g., 5 mols.) in dry ether (25 ml.) and then refluxed for 1 hr. Next morning ethyl acetate (5 ml.) and cold 3N-hydrochloric acid (25 ml.) were added and the resulting solution was extracted with ether and washed with alkali. The product (0·9 g.), crystallised from light petroleum (b. p. 80—100°), gave octadec-*trans*-11-en-9-ynol, m. p. 23—25° (lit., 30—31°) [α-naphthylurethane, m. p. 56—57° (lit., 57—57·5°)].

Dihydroxystearolic acid (1 g.), similarly reduced (7·5 mols. of lithium aluminium hydride; refluxing for 3 hr.), gave 1 : 11 : 12-*trihydroxyoctadec*-9-*yne*, m. p. 79—80° (Found : C, 72·1; H, 11·5. $C_{18}H_{34}O_3$ requires C, 72·4; H, 11·5%; microhydrogenation indicated 1·8 C:C or 0·9 C:C). Increased amounts of lithium aluminium hydride and different reflux periods did not change the nature of the product which was also obtained (m. p. 76—77°; mixed m.p. 77—79°) by performic acid oxidation of octadec-*trans*-11-en-9-ynol.

Reduction of dihydroxystearic acid gave 1 : 11 : 12-*trihydroxyoctadecane*, m. p. 126—126·5° (from ethanol) (Found : C, 71·6; H, 12·5. $C_{18}H_{38}O_3$ requires C, 71·5; H, 12·7%). The same compound was obtained by catalytic reduction of 1 : 11 : 12-trihydroxyoctadec-9-yne.

Dihydroxyoleic acid, reduced with lithium aluminium hydride, gave a small quantity of solid, m. p. 51—52°, which was probably 1 : 11 : 12-trihydroxyoctadec-*cis*-9-ene since microhydrogenation (H_2 uptake, 0·94 double bond) gave a product (m. p. 122—124°) identical with the 1 : 11 : 12-trihydroxyoctadecane described above.

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Observations on the Properties of Cetyltrimethylammonium Salts of Some Acidic Polysaccharides.

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The solubilities of the cetyltrimethylammonium salts of some mono- and poly-uronic acids and sulphated mono- and poly-saccharides are examined and compared with those of other amine (*e.g.*, 4-amino-4′-chlorodiphenyl) salts. An improved method has been developed, utilising the cetyltrimethylammonium salt as an intermediate, for the isolation, from bovine trachea, of inorganic salts of chondroitin hydrogen sulphate (suitable for the preparation of D-chondrosamine hydrochloride). The interconversion of salts of acidic polysaccharides may be achieved conveniently *via* the cetyltrimethylammonium salt. A method, based on cetyltrimethylammonium bromide (Cetavlon), for the detection of a wide range of acidic polysaccharides in paper chromatography and paper electrophoresis is described.

Cetavlon (cetyltrimethylammonium bromide) has been introduced recently as a precipitant for acidic (non-sulphated) polysaccharides (Jones, *Biochim. Biophys. Acta*, 1953, **10**, 607) and for sulphated polysaccharides (Stacey and Barker, in "Biochemistry of Nitrogen," Acad. Sci. Fennica, 1955, p. 262; Scott, *Chem. and Ind.*, 1955, **168**) since it yields water-insoluble quaternary salts with these polysaccharides; neutral polysaccharides are not precipitated by this reagent (cf. Stacey and Barker, *loc. cit.*). We now report some observations on the properties of cetyltrimethylammonium salts of certain acidic polysaccharides.

The efficiency of Cetavlon as a precipitant for sulphated polysaccharides does not appear to depend critically on the molecular size of the carbohydrate since some simple sugar sulphates, *e.g.*, 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucofuranose 3-sulphate, are precipitated. The general properties (cf. Jones, *loc. cit.*; Stacey and Baker, *loc. cit.*) of the cetyltrimethylammonium salts of mono- and poly-saccharide sulphates appear to be essentially similar. For acidic (non-sulphated) polysaccharides molecular weight is important since simple uronic acid derivatives, *e.g.*, sodium D-glucuronate, do not yield water-insoluble cetyltrimethylammonium salts.

A number of amines have been reported as precipitants for highly sulphated polysaccharides, especially for heparin, *e.g.*, benzidine (Charles and Scott, *Biochem. J.*, 1936, **30**, 1927), piperidine, *n*-pentylamine, *iso*pentylamine (Scott, Charles, and Fischer, *Trans. Roy. Soc. Canada*, 1942, V, **36**, 49), and decamethylenediamine (Lee and Berger, U.S.P. 2,561,384; *Chem. Abs.*, 1951, **45**, 10,515), but the applicability of these reagents as general precipitants for acidic polysaccharides appears not to have been studied. It is of interest that whilst the cetyltrimethylammonium salts of a range of acidic polysaccharides (Jones, *loc. cit.*; Stacey and Barker, *loc. cit.*; Scott, *loc. cit.*) have been found to be water-insoluble the corresponding salts derived from 4-amino-4′-chlorodiphenyl were found to be water-insoluble only in the case of highly sulphated polysaccharides (*e.g.*, heparin and dextran sulphates with 5—6 sulphate ester groups per tetrasaccharide unit). Polysaccharides which had less than 3 sulphate ester groups per tetrasaccharide unit [*e.g.*, de-*N*-sulphated heparin (Foster, Martlew, and Stacey, *Chem. and Ind.*, 1953, 825, 899), sodium chondroitin sulphate, and some polyuronic acids] did not give water-insoluble salts with 4-amino-4′-chlorodiphenyl (Foster and Martlew, unpublished data). It is possible that the combined use of the reagents Cetavlon and 4-amino-4′-chlorodiphenyl might be advantageous in certain cases. A further significant difference between these reagents is that the former yields a water-soluble sulphate whilst the latter may be used to precipitate sulphate ion quantitatively (Belcher, Nutten, and Stephen, *J.*, 1953, 1334). It has been pointed out (Stacey and Barker, *loc. cit.*) that separation into fractions of low and high sulphate content of a mixture of sulphated polysaccharides may be achieved by the use of sub-optimal amounts of Cetavlon.

Although the minimum number of acid functions per polysaccharide molecule necessary to give a water-insoluble cetyltrimethylammonium salt is not known precisely, it would appear to be small.

In order to assess the value of Cetavlon as a reagent for facilitating the isolation of salts of chondroitin hydrogen sulphate from bovine trachea a series of experiments were made in which fresh and " dried " trachea (see Experimental section) were subjected to various extraction procedures. The results are listed in Table 1. The general method employed

TABLE 1. *Analytical and other data on the various preparations of salts of chondroitin hydrogen sulphate.*

Sample	Extractant	Yield (g.)	Moisture (solvent) (%)	N (%) [a]	S (%) [a]	*N*-Acetyl (%) [a]	$[\alpha]_D^{21}$ in H_2O	Salt
			From fresh trachea					
I	NaOH	3·05 [c]	17·73	—	6·3	8·0	−18·6°	Na
II [b]	NaOH	3·20 [c]	20·87	2·15	6·1	8·4	−21·0	Na
			From dried trachea					
III	NaOH	3·45	18·07	2·1	5·6	7·45	−17·4	Na
IV	NaOH	3·00	19·11	2·1	5·5	7·8	−15·6	Na
V	$CaCl_2$	0·45	17·39	3·4	4·2	7·0	−17·6	Na
VI	$CaCl_2$	1·28	17·37	2·9	5·0	7·0	−21·8	Na
VII	NaCNS	0·70	17·42	3·9	4·3	6·1	−29·4	Na
VIII	NaCNS	0·35	15·49	3·6	4·3	5·95	−25·5	Na
IX	$Ba(OH)_2$	2·10	17·69	2·0	5·45	7·8	−21·4	Ba
X	NaOH	—	18·81	2·1	5·7	7·4	−16·3	Ba

Col. 5—9: data determined on moisture (solvent)-free salts. [a] Calc. for sodium chondroitin sulphate ($C_{14}H_{19}O_{14}NSNa_2$): N, 2·8; S, 6·4; *N*-Ac, 8·55; for barium chondroitin sulphate ($C_{14}H_{19}O_{14}NSBa$): N, 2·4; S, 5·4; *N*-Ac, 7·24%. [b] Sodium salt (II) was subjected to deproteinization. [c] Yields are calculated and approximate.

was to precipitate cetyltrimethylammonium chondroitin sulphate under suitable conditions after the extraction procedure, and then to convert the quaternary salt into other required salts.

In the case of " dried " trachea hot dilute aqueous sodium hydroxide (Bray, Gregory, and Stacey, *Biochem. J.*, **1944**, **38**, 142) proved to be the most efficient extractant in that it afforded the highest yield of sodium chondroitin sulphate (Samples III and IV). The analytical data indicated that the salts (III) and (IV) contained some protein. Extraction of fresh trachea under similar conditions gave almost the same yield of sodium chondroitin sulphate (I) which appeared to have lower protein content than the salts (III) and (IV). Application of a standard deproteinisation procedure to the salt (I) reduced easily and substantially the traces of protein, to give the salt (II). No special precautions were taken to exclude oxygen in the hot alkaline extractions and it is not unlikely that the sodium salts (I)—(IV) had suffered some degradation (cf. Blix and Snellman, *Arkiv Kemi Mineralog. Geol.*, **1945**, **19**, No. 32, 1; Bottle, Gilbert, Greenwood, and Saad, *Chem. and Ind.*, **1953**, 541). Such degradation is relatively unimportant if the mucopolysaccharide is to be further degraded, for example, to chondrosine (Levene and La Forge, *J. Biol. Chem.*, **1913**, **15**, 69, 155; Levene, *ibid.*, **1941**, **140**, 267) or D-chondrosamine hydrochloride (cf. *inter al.*, Levene and La Forge, *loc. cit.*; Stacey, *J.*, **1944**, 272; Gardell, *Acta Chem. Scand.*, **1951**, **5**, 195).

The use of Cetavlon in the above extraction procedure constitutes an improvement in the method of isolation, from bovine trachea, of salts of chondroitin hydrogen sulphate suitable for studies of degradation and for the preparation of D-chondrosamine hydrochloride. On the basis of the detailed study a simplified extraction procedure has been developed.

The sulphur percentages in Table 1 were obtained by the application of a modified method of ester-sulphate determination developed in these laboratories by Belcher and Fildes (unpublished work). Hydrolysis of the sulphate groups was effected under oxidising conditions (nitric acid) and thereafter the released sulphate ions were determined by a standard procedure. The method was found to be convenient and of particular value for the determination of sulphur in sulphated carbohydrates.

There has been no report of the nature and composition of the quaternary salts of acidic polysaccharides. The isolation of cetyltrimethylammonium and cetylpyridinium chrondroitin sulphates gave no difficulty and the quaternary salts were found to have low (<0·5%) ash contents. This observation, which indicates the almost complete replacement of other cations by the cetyltrimethylammonium or cetylpyridinium ion, supplements that of Scott (*loc. cit.*), who found that the titration of sulphate groups, in dextran sulphate, with Cetavlon corresponded to stoicheiometric salt formation. Scott (*loc. cit.*) reported a flocculation end point in these titrations, which we have noted also with salts of chondroitin sulphate. The low ash content of the quaternary salts also indicates that the interconversion of salts of an acidic polysaccharide (as, for example, in the conversion of sodium into barium chondroitin sulphate before preparation of D-chondrosamine hydrochloride) may be achieved conveniently *via* the cetyltrimethylammonium salt. Ammonium chondroitin sulphate prepared from the sodium salt in this manner had a very low (0·06%) ash content. By a similar procedure heparin (sodium salt) was converted *via* the benzidine salt into an ammonium salt with 0·7% ash content (Charles and Scott, *loc. cit.*; cf. Wolfrom, Weisblat, Karabinos, McNeely, and McLean, *J. Amer. Chem. Soc.*, 1943, **65**, 2077).

The yields of sodium chondroitin sulphate (V and VI) obtained on extraction of dried trachea with aqueous calcium chloride (cf. Meyer and Smyth, *J. Biol. Chem.*, 1937, **119**, 507) were much lower than in extraction with hot alkali, and the salts contained significant amounts of protein. It appears that appreciable contamination with protein did not increase the solubility of the cetyltrimethylammonium salt in water. Salts (VII and VIII) of essentially similar composition were obtained when aqueous sodium thiocyanate (cf. Snellman, Jensen, and Sylvén, *Nature*, 1948, **161**, 639) was used as extractant. The use of hot aqueous baryta as an extractant gave barium chondroitin sulphate (IX) with essentially the same elemental composition as, but in lower yield than, the corresponding salt (X) obtained after sodium hydroxide extraction.

Few reagents have been reported for the detection of polysaccharides in paper chromatography and ionophoresis. Aniline oxalate has been used to detect certain neutral polysaccharides (Preece and Hobkirk, *Chem. and Ind.*, 1955, 257) but a satisfactory general method for the detection of acidic polysaccharides has not been described. Sulphated polysaccharides may be located after paper electrophoresis by means of Toluidine-blue (Rienits, *Biochem. J.*, 1953, **53**, 79) and the same reagent and also Azure I have been used similarly in paper chromatography (Kerby, *Proc. Soc. Exp. Biol. Med.*, 1953, **83**, 263; Ricketts, Walton, and Saddington, *Biochem. J.*, 1954, **58**, 532; cf. Ball and Jackson, *Stain Technol.*, 1953, **28**, 33). The detection of acidic (non-sulphated) polysaccharides with Toluidine-blue is unsatisfactory. We have found that Cetavlon may be used to detect satisfactorily a wide range of acidic polysaccharides in paper chromatography and in ionophoresis in acetate (pH 5·0) and borate (pH 10·0; cf. Foster, *J.*, 1953, 982) buffer systems. After chromatography or ionophoresis the acidic polysaccharides on the paper were converted into the cetyltrimethylammonium salts by treatment with Cetavlon. After removal of excess of the detergent the insoluble cetyltrimethylammonium polysaccharide salts were detected with Bromocresol-purple. In this manner sodium alginate, luteic acid, *Azotobacter chroococcum* polysaccharide, gum arabic, gum tragacanth, hyaluronic acid, sodium chondroitin sulphate, heparin (sodium salt), and barium 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucofuranose 3-sulphate were found to be located readily.

The observation that cetyltrimethylammonium chondroitin sulphate was soluble in alcohols up to *n*-pentyl alcohol prompted an examination of the behaviour of the quaternary salt in paper chromatography. It was found that with the organic phase of acidic (butanol–water–acetic acid, 4 : 5 : 1), neutral (butanol–ethanol–water, 4 : 1 : 5) and basic (butanol–ethanol–water–ammonia, 40 : 10 : 49 : 1) solvent systems, dissociation of the quaternary salt occurred. The polysaccharide was retained near the origin and the cetyltrimethyl ammonium moiety ran just behind the solvent front.

Experimental

Preparation of "Dried" Trachea.—Fresh bovine trachea (850 g.) were freed as completely as possible from adhering fat, flesh, and extraneous matter, minced, and defatted by exhaustive

extraction with acetone at room temperature. The material (200 g.) obtained after air-drying is subsequently referred to as " dried " trachea (moisture content, 15·94%).

Extraction of " Dried " Trachea.—(a) *With* N-*sodium hydroxide* (Bray, Gregory, and Stacey, *loc. cit.*). Dried trachea (30 g.) was extracted at 70° with N-sodium hydroxide (1 l.) for 30 min. The cooled, turbid solution was neutralised with acetic acid and dialysed against running tap-water for 2 days, and insoluble material then removed by centrifugation. Aqueous cetyltrimethylammonium bromide (Cetavlon; 2—20% w/v) was added to the centrifugate until precipitation of the quaternary salt was complete (flocculation end point). The precipitate was collected by centrifugation, washed twice with distilled water, and then dissolved in the minimum volume of aqueous sodium chloride (10% w/v). Sodium chondroitin sulphate was precipitated by the addition of ethanol (1—2 vols.). The polysaccharide was collected by centrifugation and dissolved in water, and the solution dialysed against running tap-water for 2 days; the dialysate was then passed down a column (25·5 × 2·5 cm.) of Zeocarb cation exchanger (sodium-salt form), and the sodium salt (III) isolated from the eluate by freeze-drying.

In a second extraction the above procedure was repeated with the omission of the first dialysis stage to give the sodium salt (IV).

(b) *With* 10% *calcium chloride* (Meyer and Smyth, *loc. cit.*). Dried trachea (30 g.) was extracted with aqueous calcium chloride (300 ml.; 10% w/v) by shaking at room temperature for 1 day. Two consecutive extracts were combined and after dialysis against running water for 2 days they were worked up as in (a), to give the sodium salt (V).

The residue remaining from the above extractions was further extracted with aqueous calcium chloride during 10 days and then worked up as above to give the sodium salt (VI).

(c) *With* 10% *sodium thiocyanate.* Dried trachea (30 g.) was extracted with aqueous sodium thiocyanate (300 ml.; 10% w/v) and the extracts were worked up as for the calcium chloride extraction, to give the sodium salts (VII) and (VIII) from two combined 24-hr. extractions and from a 10-day extraction respectively.

(d) *With* N-*barium hydroxide.* Dried trachea (30 g.) was extracted with N-barium hydroxide (500 ml.) at 70° for 30 min. The cooled solution was neutralised by the addition of solid carbon dioxide and clarified by centrifugation. The clear centrifugate was treated with aqueous Cetavlon (2—20% w/v), and the precipitated quaternary salt was collected and washed as in (a). Thereafter the quaternary salt was dissolved in aqueous barium chloride (10% w/v; 70 ml.), and barium chondroitin sulphate precipitated by the addition of alcohol (1—2 vols.). The barium salt was dissolved in water, converted into the insoluble quaternary salt, and reconverted into the barium salt as described above. An aqueous solution of the product was dialysed against running water for 2 days and the barium salt (IX) isolated from the dialysate by freeze-drying.

A sample of sodium chondroitin sulphate prepared from fresh trachea (see below) was converted into the cetyltrimethylammonium salt and thence into the barium salt (X) as described above.

Extraction of Fresh Trachea with N-*Sodium Hydroxide.*—Cleaned and minced bovine trachea (540 g.; equivalent to *ca.* 130 g. of " dried " trachea) was extracted as in (a). Thereafter the solution was neutralised with acetic acid and then treated with barium carbonate (100 g./l.) at 100° for 6 hr. Insoluble material was removed by centrifugation and washed with water, and the combined centrifugates were concentrated (1600 ml.). Aqueous Cetavlon (2—20% w/v) was added until precipitation of the quaternary salt was complete, the precipitate collected (centrifuge), and dissolved in the minimum volume of aqueous sodium chloride (10% w/v), and sodium chondroitin sulphate precipitated by the addition of alcohol (1—2 vols.). The precipitate (33 g.) was collected, washed with alcohol and then ether, and dried. Attempts to remove or decrease the protein content of this salt, (1) by passage of its aqueous solution through a Celite column (*ca.* 15 × 2 cm.) and (2) by repeated conversion into the cetyltrimethylammonium salt, thorough washing, and reconversion into the sodium salt, were unsuccessful. An aqueous solution of a portion (5·0 g.) of the product was dialysed against running water for 2 days and the sodium salt (I) treated and isolated as in (a). A similar amount was substantially freed from traces of protein by shaking seven times with chloroform–pentyl alcohol (Sevag, *Biochem. Z.*, 1934, **273**, 419), and the sodium salt (II) was isolated as described above.

The sodium salts (I) and (II) were found to be suitable for the preparation of D-chondrosamine hydrochloride after their conversion into the barium salts by the general method described below.

The yields and analytical data for the salts (I)—(X) are recorded in Table 1. *N*-Acetyl

determinations were carried out by using toluene-*p*-sulphonic acid and the digestion conditions described by Wolfrom *et al.* (*loc. cit.*), and the method for acetic acid determination described by Belcher and Godbert (" Semi-micro Quantitative Organic Analysis," Longmans, Green and Co., 1954, p. 161). Sulphur was determined according to the method of Belcher and Fildes (*loc. cit.*): A sample of the sulphated polysaccharide (30—50 mg.) was hydrolysed by boiling under reflux with 8N-nitric acid (5 ml.) for 1 hr. Thereafter the nitric acid was evaporated and the last traces removed by co-distillation with hydrochloric acid. The residue was dissolved in 0·05N-hydrochloric acid (50 ml.) and barium sulphate was precipitated, collected, and determined by the method of Belcher, Gibbons, and West (*Chem. and Ind.*, 1954, 127, 850).

Simplified Procedure for the Extraction of Salts of Chondroitin Hydrogen Sulphate from Bovine Trachea.—Fresh, cleaned and minced trachea was extracted with N-sodium hydroxide at 70° for 30 min. Thereafter the solution was neutralised with acetic acid and clarified by centrifugation. Aqueous Cetavlon (2—20% w/v) was added to the centrifugate until precipitation of the quaternary salt was complete. The precipitate was collected and washed twice with water (centrifuge). Conversion of the quaternary salt into other salts was effected by its dissolution in an aqueous solution of the appropriate chloride (*e.g.*, Na, Ba, Ca, NH_4) and precipitation by the addition of alcohol (1—2 vols.). The precipitate was then washed with aqueous ethanol (80%) until free from chloride ion. Barium chondroitin sulphate prepared in this manner contained a trace of proteinaceous material but was suitable for the preparation of D-chondrosamine hydrochloride.

Isolation of the Cetyltrimethylammonium and Cetylpyridinium Salts of Chondroitin Hydrogen Sulphate.—A solution of sodium chondroitin sulphate (5 g.) in water (100 ml.) was treated with aqueous Cetavlon (20% w/v) until precipitation of the cetyltrimethylammonium chondroitin sulphate was complete. Under these conditions the quaternary salt was precipitated as a flocculent solid but on addition of excess of Cetavlon it became syrupy. The precipitate was collected by centrifugation. A portion was washed twice with water, dissolved in ethanol, and precipitated as a wax-like solid (A) by the addition of ether. A second portion was washed thrice with a little Cetavlon solution and then treated as above. A wax-like solid (B) was again obtained. If, however, the initial precipitate was washed with acetone and then with ether, the quaternary salt was obtained as a fine white powder (C). Cetylpyridinium chondroitin sulphate (D) was also isolated in this manner as a fine white powder. Some analytical data on A—D are included in Table 2. The quaternary salts A—D were soluble in alcohols up to

TABLE 2.

	A	B	C	D
Moisture (solvent) content (%)	16·35	13·51	7·2	9·1
Ash (calc. on dry solid) (%)	0·41	0·39	0·42	0·41

n-pentanol but were insoluble in other common organic solvents, aqueous ammonia, and acetic acid.

Detection of Acidic Polysaccharides after Chromatography and Electrophoresis on Paper.—(a) *On the paper.* Chromatograms (Whatman No. 1 paper) were examined which had been irrigated with a propan-1-ol–water (1 : 1) solvent system. Ionophoretograms (Whatman No. 3 paper) were examined which had been run in acetate buffer (pH 5·00; 19·04 g. of sodium acetate trihydrate and 3·6 g. of acetic acid per l.) and borate buffer [pH 10·0; 19·77 g. of boric acid and 16·0 g. of sodium hydroxide per 4 l. (cf. Foster, *loc. cit.*)] systems. The method of detection was the same in each case. The dried (100—110°) paper was dipped in aqueous Cetavlon (1% w/v), excess of reagent removed by immediate and thorough washing with hot, running tap water for 5—10 min. (the minimum time depends on the thickness of the paper), and the paper dried at 100°. Thereafter the paper was sprayed with ethanolic bromocresol-purple (0·04% w/v) to which dilute aqueous sodium hydroxide had been added until the solution began to assume a reddish tinge. The locations of the polysaccharides were indicated by blue spots (which did not fade appreciably on storage of the paper) on a pale yellow background. This procedure was used for the substances listed on p. 3790.

Incomplete washing of the paper led to a final overall blue colour on spraying with bromocresol-purple, and the polysaccharide locations were then not easily discernible. In this case the paper was dipped in N-acetic acid, washed thoroughly, and dried. On heating to 100° green spots appeared on a pale yellow background. The spots tended to fade but could be regenerated by heat. The acetic acid treatment may be repeated if necessary.

(b) *After elution.* In paper chromatography of sodium chondroitin sulphate an alternative

method of detection was as follows: the chromatogram was dissected into strips (the width dependent on the distance migrated) at right angles to the direction of movement of the acidic polysaccharide, and the strips were separately eluted with boiling water (cf. Rienits, *loc. cit.*). The extracts were treated with aqueous Cetavlon (2% w/v), and the presence of acidic polysaccharide was indicated by the development of turbidity or the formation of a precipitate.

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The Molecular Polarisation and Association of Some Hydroxylic Compounds in Benzene Solution.

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The dielectric constants, specific volumes, and refractive indices of benzene solutions of *n*- and *tert.*-butyl and benzyl alcohols, diphenylmethanol, and phenol have been measured over the concentration range 0·2—7% (w/w), and the apparent molecular polarisations of the solutes at each concentration evaluated. Cryoscopic measurements have also been made on benzene solutions of *n*- and *tert.*-butyl alcohols and of diphenylmethanol. For each compound the course of the molecular polarisation–concentration curve is anomalous compared with that for a non-associating solute, but it has been interpreted in terms of the geometrical form of the molecules concerned and their association. Owing to this anomalous behaviour the results cannot be extrapolated to zero concentration so accurately as for normal solutes. From the measurements at the lowest concentrations, however, and the total distortion polarisation being assumed to be equal to the molecular refraction for the Na-*D* line, the values obtained for the apparent dipole moments of the monomeric forms in benzene solution are: *n*-butyl alcohol 1·69, *tert.*-butyl alcohol 1·69, diphenylmethanol 1·62, benzyl alcohol 1·67, and phenol 1·45 D.

OWING to the strong tendency of alcohols to associate, their solutions in non-polar solvents show a variation of dielectric polarisation with concentration which is anomalous compared with that for solutions of a normal non-associating solute. The most firmly established feature is that the values of the molecular polarisation (P_2) of certain alcohols, based on the molecular weight of the monomeric alcohol and calculated on the assumption that the molecular polarisation of the solvent remains constant, pass through a maximum, often within the concentration range 40—60 mol.-% alcohol.

The evidence regarding the behaviour at low concentrations is more conflicting. Smyth and Stoops (*J. Amer. Chem. Soc.*, 1929, **51**, 3312), Hennings (*Z. phys. Chem.*, 1935, **28**, *B*, 267), Müller and Mortier (*Physikal. Z.*, 1935, **36**, 371), and Hoecker (*J. Chem. Phys.*, 1936, **4**, 431) all found that the P_2 values of ethyl or *n*-butyl alcohol decrease with increasing concentration and pass through a minimum below 1 mol.-%, before increasing to the maximum value. On the other hand, Maryott (*J. Amer. Chem. Soc.*, 1941, **63**, 3079) was unable to find any such minima. Smyth and Stoops also reported that the P_2 values for various alcohols at concentrations below about 1 mol.-% in hexane or heptane solution appeared to increase with rise of temperature, instead of decreasing as would be expected on the Debye theory. Since the dipole moment of a monomeric alcohol molecule should be almost independent of the orientation of the hydroxyl group with respect to the carbon chain, such behaviour is possible only if P_2 for the unassociated molecules is greater than its apparent value for the associated molecules.* Even then it should occur only at concentrations at which the degree of association is fairly high, so that there is an appreciable

* Here, as elsewhere in this paper, P_2 for a compound in the associated state is taken as the value based on the molecular weight of the monomer.

increase in the proportion of non-associated molecules when the temperature is raised. Smyth and Stoops's extrapolation of their results, however, suggests that the increase in P_2 with rise of temperature becomes a maximum at zero concentration, which seems to be impossible, as the $P_{2\infty}$ value should apply to the unassociated molecules.

Before making a quantitative study of the marked changes in the apparent molecular polarisation of alcohols produced by the addition of small concentrations of nitrogenous bases (Cleverdon and Smith, *Chem. and Ind.*, 1948, 23), it was necessary to reinvestigate the molecular polarisations of certain alcohols at low concentrations in benzene. The compounds chosen were *n*- and *tert.*-butyl alcohols, benzyl alcohol, and diphenylmethanol, and, since behaviour similar to that of the alcohols might be expected with phenol, some measurements on this compound have also been included. As the apparently anomalous P_2 values obtained by some workers for solutions of low concentration could have arisen through the use of incorrect values for the dielectric constant or density of the solvent relative to the values for the solutions, some series of independent measurements have been made upon each of the systems other than that involving benzyl alcohol. In these, four different forms of apparatus have been used to determine the dielectric constants of the solutions relative to that of benzene, and some series of measurements have been extended to very low concentrations of the hydroxylic compounds.

The results have shown that neither the dielectric constants (ε) nor the specific volumes (v) of the solutions vary simply with concentration. Curves were therefore drawn of the variation of ε, v, and the refractive index (n) of the solutions with the weight fraction of solute (w), and from these the values at certain specific concentrations shown in

TABLE 1. *Polarisation and association data for hydroxylic compounds in benzene solution.*

$100w$	$10^4\Delta\varepsilon$	$10^5\Delta v$	$10^4\Delta n_D$	P_2 (c.c.)	$[R_D]$ (c.c.)	x	$100w$	$10^4\Delta\varepsilon$	$10^5\Delta v$	$10^4\Delta n_D$	P_2 (c.c.)	$[R_D]$ (c.c.)	x
n-Butyl alcohol							*tert.*-Butyl alcohol						
0·5	192	65	− 7	81·4	21·8	1·06	0·5	183	101	− 8	80·6	22·5	1·03
1·0	392	128	−13	82·3	22·1	1·12	1·0	367	200	−15	80·5	22·9	1·08
1·5	598	190	−20	83·0	22·0	1·22	1·5	550	297	−23	80·4	22·6	1·16
2·0	809	250	−27	83·5	21·9	1·33	2·0	734	392	−30	80·2	22·8	1·24
2·5	1022	309	−33	83·8	21·9	1·43	2·5	917	485	−38	79·9	22·6	1·33
3·0	1239	368	−39	84·1	22·0	1·53	3·0	1096	576	−45	79·4	22·6	1·40
4·0	1672	483	−52	84·3	21·9	1·74	4·0	1440	754	−60	78·3	22·6	1·56
5·0	2107	595	−64	84·2	22·0	1·91	5·0	1770	929	−75	77·2	22·5	1·71
6·0	2556	710	−75	84·3	22·1	2·07	6·0	2091	1100	−89	76·1	22·5	—
7·5	3262	876	−92	84·6	22·1	2·32	7·0	2411	1270	−103	75·2	22·6	—
Diphenylmethanol													
0·5	90	−123	5	111·3	57·0	1·00	3·0	558	−738	26	112·5	57·8	1·06
1·0	181	−246	9	111·6	58·1	1·00	4·0	754	−984	34	112·9	57·7	1·11
1·5	273	−369	14	111·8	58·2	1·00	5·0	953	−1230	43	113·2	57·6	1·17
2·0	367	−492	18	112·1	58·0	1·02	6·0	1156	−1476	51	113·5	57·6	—
2·5	462	−615	22	112·3	57·7	1·04	7·0	1361	−1722	—	113·6	—	—
Phenol													
0·5	131	−112	2	72·0	27·6	—	3·0	870	−672	15	75·8	28·1	—
1·0	267	−224	5	72·7	28·1	—	4·0	1200	−896	20	77·1	28·1	—
1·5	409	−336	7	73·5	27·9	—	5·0	1550	−1120	25	78·3	28·1	—
2·0	558	−448	10	74·4	28·1	—	6·0	1919	−1344	30	79·3	28·1	—
2·5	710	−560	12	75·0	28·0	—	7·0	2306	−1568	35	80·4	28·0	—
Benzyl alcohol													
1·1340	341	−208	5	91·5	32·5	—	5·6065	1901	−1051	24	96·3	33·0	—
2·5749	817	−483	11	93·9	32·6	—	7·1772	2492	−1353	30	96·7	32·8	—
3·7120	1216	−702	16	95·2	32·7	—	7·6993	2689	−1451	33	96·8	32·7	—
4·6753	1557	−886	20	95·6	32·6	—							

Table 1 were found. The values of P_2 calculated from these figures lie satisfactorily upon the P_2–w curves derived directly from the measurements on the individual solutions.

Table 1 also includes the results of the one series of measurements upon benzyl alcohol. After this had been completed, results for the same temperature were recorded by Buckingham, Holland, and Le Fèvre (*J.*, 1954, 1646). As the agreement between the two

groups of results was remarkably close, no further measurements on this compound were deemed necessary.

To assist in correlating the results with the association of the hydroxylic compounds, cryoscopic measurements have been made on dilute solutions of *n*- and *tert.*-butyl alcohol and of diphenylmethanol in benzene. The cryoscopic constant of benzene being assumed to be 5·2° kg.$^{-1}$, the results have been used to evaluate the mean degree of complexity of the alcohol molecules. Interpolated values for various concentrations are shown as x in Table 1: although these extend beyond the range over which ideal behaviour can be expected, the figures obtained should be of the correct order of magnitude. The results for *n*-butyl alcohol are in fair agreement with the measurements of Giacolone (*Gazzetta*, 1942, **72**, 378).

Discussion of Results

Wolf and Herold (*Z. phys. Chem.*, 1934, **27**, *B*, 58) pictured the association of two alcohol molecules as occurring in all possible ways ranging between the two extreme configurations (I) and (II) in which the dipoles are parallel and antiparallel, respectively, and they accounted for the variation of P_2 with concentration then reported by supposing the solutions to contain some double and triple molecules with mean dipole moments respectively less and greater than that of a single molecule. On the other hand, Hückel and Schneider (*ibid.*, 1940, **47**, *B*, 227) postulated the existence of two types of double alcohol molecules, approximating to the configurations (I) and (II), steric factors determining which of these predominates in any particular case.

Modern theories of hydrogen bonding render these completely parallel and completely antiparallel arrangements of the dipoles in the associated molecules improbable. To take the simplest possible case, let us suppose that the dipole in the single alcohol molecule acts along the bisector of the C–O–H angle, and that the latter is equal to the tetrahedral angle.

In (III) and (IV) the Bonds O···H and R—O are in a plane perpendicular to the paper.

Then, if the two oxygen atoms in a double molecule are collinear with the hydrogen atom bonding them, and rotation is possible about the O–H–O axis, the molecular configurations leading to maximum and minimum resultant moment are those shown in (III) and (IV), respectively. In (III) the dipoles are parallel, and so the moment of the dimer is double that of the monomer, whereas in (IV) the dipoles are inclined at the tetrahedral angle and so the resultant moment is $2/\sqrt{3}$ that of the monomer. The apparent orientation polarisations in the two cases are therefore respectively twice and two-thirds of that of the monomer, so, if rotation is free, P_2 should be increased by the formation of dimeric molecules. If the groups R are bulky, however, as in *tert.*-butyl alcohol, steric factors will cause configurations near to (IV), where the groups R are more remote from one another, to predominate, so the value of P_2 for the dimeric molecules is not likely to be much greater than for the monomeric molecules. Further association to trimeric molecules can lead to configurations with moments ranging from still higher values to nearly zero, but, in the absence of any ordered arrangement, probability considerations make it unlikely that P_2 will attain a very high value. When steric factors enter, adjacent dipoles will be partially opposed, as in (IV), and so P_2 may well fall below the value for the monomeric state. Similar arguments apply when more complex association is involved.

The results for *n*-butyl alcohol indicate that P_2 increases sharply with increasing concentration up to about 2% (w/w), after which it changes less, remaining almost constant between 3 and 6% (w/w). As the value at zero concentration corresponds with the monomeric alcohol, it can be inferred that P_2 is greater for the dimeric than for the monomeric form, as is to be expected if free rotation occurs about the O–H–O axis. The fact that the

increase in P_2 with increasing concentration does not persist much beyond 2% (w/w) suggests that association into more complex forms then becomes appreciable and that this causes no further increase in P_2. In view of these observations it is at first sight rather surprising that the cryoscopic measurements indicate that at a concentration of 2% (w/w) the mean molecular complexity at the freezing point of benzene is 1·33, whilst at 5% it is still only 1·9. At the temperature of the polarisation measurements (25°) the complexity will be lower.

Some light is thrown on this matter, however, by the infrared spectra of carbon tetrachloride solutions of ethyl alcohol, in which the 3638, 3523, and 3300 cm.$^{-1}$ frequencies have been attributed by Errera, Gaspart, and Sack (*J. Chem. Phys.*, 1940, **8**, 63) to the vibrations of hydroxyl groups in single, double, and more highly associated molecules, respectively. Their absorption curves suggest that at 20° the proportion of polymer in 0·125 and 0·25% solutions is small, but that at concentrations of 0·5% and higher, absorption by the polymer exceeds that by the dimer, although the most intense band is still that due to the monomer. If the behaviour of *n*-butyl alcohol follows a similar pattern it seems likely that increase of concentration between 2 and 6% (w/w) is accompanied by an increase in the proportion of polymeric molecules and a decrease in the proportion of monomer, the proportion of dimer only increasing slightly and still remaining relatively small. If P_2 for the polymer is about equal to or slightly less than that of the monomer, such behaviour would account for the course of the P_2–w curve up to about 6% (w/w).

This interpretation suggests that the alcohol tends to exist mainly as monomeric molecules and polymeric aggregates. This is not improbable, since the participation of the hydrogen atom of a hydroxyl group in a hydrogen bond will lead to an increased electron density at the oxygen atom. Hence, steric factors permitting, its chance of becoming "bonded" by the hydrogen atoms of another hydroxyl group should be increased as compared with that of the oxygen atom of a monomeric molecule.

At concentrations above 6% (w/w), P_2 for *n*-butyl alcohol rises again with increasing concentration, and, outside the range studied here, various observers have reported a considerable increase in P_2 between about 10 and 40%, followed by a gradual fall to the value for the pure alcohol. The increase may be due to the establishment of some degree of order in the alcohol aggregates, so that the individual dipoles have less tendency to cancel one another out, whilst the fall in P_2 at very high concentrations can be associated with the inter-linking of the aggregates and consequent hindrance to rotation of the type discussed by Oster and Kirkwood (*J. Chem. Phys.*, 1943, **11**, 175).

In view of the variations of P_2 with concentration, it is interesting that the molecular refraction of *n*-butyl alcohol does not vary appreciably with its extent of association, but remains very close to the value for the pure liquid (22·14 c.c.; Vogel *et al.*, *J.*, 1948, 1817).

At first sight the variation of P_2 with concentration for benzene solutions of *tert.*-butyl alcohol seems very different from that for solutions of *n*-butyl alcohol. P_2 remains almost constant up to about 2% (w/w) of alcohol, and then decreases gradually with increasing concentration. The cryoscopic measurements indicate that over the concentration range studied *tert.*-butyl alcohol is only slightly less associated than is the *n*-isomer. The analogy between the behaviour of the two compounds becomes clear, however, if it is assumed that, owing to steric factors, the dimer of *tert.*-butyl alcohol has a mean P_2 value approximately equal to that of the monomer, but that further increase in complexity leads to a decrease in P_2.

Both for *n*- and for *tert.*-butyl alcohol the specific-volume determinations indicate that the partial molar volumes of the alcohols decrease with increasing concentration. In each case this decrease is most rapid at concentrations below 2% (w/w), the values at the highest concentrations studied being only slightly higher than for the pure liquids.

For the other three solutes studied the variations of P_2 with concentration are similar in type but differ in degree. In each case P_2 increases with increasing concentration but the rate of change becomes progressively less the greater the concentration. The cryoscopic measurements indicate that diphenylmethanol is much less associated in benzene solution than is either *n*- or *tert.*-butyl alcohol at similar concentrations. As in this case the increase of P_2 with increasing w is only small, the polarisation results can be explained by

supposing that P_2 is appreciably higher for dimeric molecules than for the monomer, but that further increases in complexity have little effect on P_2.

Although the sharp rise in the P_2–w curves for benzyl alcohol and phenol suggests that the greatest increase in P_2 occurs on passing from monomeric to dimeric molecules, the fact that P_2 continues to increase with increasing w over the whole concentration range studied makes it probable that for these compounds the mean value of P_2 for the polymeric molecules may always be greater than for the monomer. The difference between this behaviour and that of the butyl alcohols indicates the possibility that the presence of the aromatic ring may induce some degree of order in the aggregates even at relatively low concentrations.

The curvature of the P_2–w and ε–w plots for all the systems studied, and of the v–w plots for *n*- and *tert.*-butyl alcohol, renders the extrapolation of these results to zero concentration less exact than for most solutes. The number of series of measurements carried out, however, has made possible a fairly accurate estimate of the gradients of these curves at zero concentration, and from these the dipole moments of the monomeric molecules in benzene solution have been derived. The results are shown in Table 2, together with the

TABLE 2. *Dipole moments in benzene solution.*

	α	β	ν	$P_{2\infty}$ (c.c.)	$[R_D]_2$ (c.c.)	μ (D)	Previous values
n-Butyl alcohol	3·77	0·133	−0·40	80·7	22·0	1·69	1·62—1·74 [a]
tert.-Butyl alcohol ...	3·65	0·206	−0·44	80·7	22·6	1·69	1·55—1·66 [a]
Diphenylmethanol ...	1·78	−0·246	0·27	110·8	57·7	1·62	1·64 [b]
Benzyl alcohol	2·90	−0·188	0·12	89·8	32·7	1·67	1·68—1·69 [a] 1·67$_5$ [c]
Phenol	2·55	−0·224	0·15	71·0	28·0	1·45	1·5—1·7 [a]

α, β, and ν are the limiting values, at zero concentration, of $\delta\varepsilon/\delta w$, $\delta v/\delta w$, and $\delta n^2/\delta w$, respectively. References: [a] Weedon, "Massachusetts Institute of Technology Tables," Technology Press, Cambridge, Mass., 1948; [b] Cleverdon and Smith, *J.*, 1951, 2321; [c] Buckingham, Holland, and Le Fèvre, *J.*, 1954, 1646.

parameters from which they have been computed and indications of the ranges covered by previous values for benzene solutions. The wide variation of the moments previously reported for *n*- and *tert.*-butyl alcohol reflects the varied interpretations of measurements on solutions of low concentration. The moment for diphenylmethanol previously recorded was slightly higher than that now reported because it was erroneously supposed that $\Delta\varepsilon/w$ and P_2 were approximately linear with w. The value now found for phenol in benzene is appreciably lower than has previously been reported, principally because the rapid fall of P_2 with decreasing concentration seems to have been largely neglected in the earlier evaluations. The new value, however, falls much better into line with the moment for the vapour (1·40 D; Groves and Sugden, *J.*, 1937, 1782), particularly as the dipole moment of anisole appears to be *lower* in benzene solution than in the vapour.

EXPERIMENTAL

Materials.—Benzene was purified and dried as described by Few and Smith (*J.*, 1949, 753). "Laboratory reagent" *n*- and *tert.*-butyl alcohol were refluxed for 3 hr. over freshly ignited calcium oxide and then further refluxed for some hours over calcium metal. They were finally distilled through a 20-plate column under anhydrous conditions. Different batches had closely concordant physical properties. *n*-Butyl alcohol had b. p. 117·8°/760 mm., d_4^{25} 0·80575, n_D^{25} 1·3973—1·3974 (Timmermans, "Physical Constants of Pure Organic Compounds," Elsevier, New York, 1950, gives b. p. 117·8—118·0°/760 mm., d_4^{25} 0·80567—0·80572, n_D^{25} 1·3970—1·3974). *tert.*-Butyl alcohol had m. p. 25·54°, b. p. 82·5°/763 mm., d_4^{25} 0·7811, n_D^{25} 1·3851 (Timmermans, *op. cit.*, gives b. p. 82·45°/760 mm., and interpolation of his data leads to d_4^{25} 0·7814, n_D^{25} 1·3851). "Laboratory reagent" benzyl alcohol was redistilled twice, the middle fraction being retained in each distillation. The sample used had b. p. 203·5°/748 mm., d_4^{25} 1·04157, n_D^{25} 1·5375 (Timmermans gives b. p. 205·25—205·45°/760 mm., d_4^{25} 1·04156). "Laboratory reagent" diphenylmethanol was recrystallised several times from petrol (b. p. 60—80°) and stored over phosphoric oxide: it had m. p. 66·4°. "Separate crystal" phenol was distilled twice at atm.

pressure, the initial fractions being rejected, and was used immediately; it had b. p. 182°/763 mm. (Timmermans gives b. p. 181·75—182·2°/760 mm.).

Apparatus and Methods.—A few of the earlier dielectric constant measurements were carried out with an apparatus similar to that described by Le Fèvre and Rayner (*J.*, 1938, 1921), and the remainder with the resonance apparatus and two forms of the heterodyne heat apparatus described by Few, Smith, and Witten (*Trans. Faraday Soc.*, 1952, **48**, 211). Specific volumes were determined with pyknometers of 8—10 c.c. capacity. Some of the refractive indices were determined with a Pulfrich refractometer and the remainder with an Abbé refractometer. All these measurements were made at 25·0°.

Cryoscopic measurements were made in an apparatus of the Beckmann type, through which a stream of dry nitrogen, saturated with the vapour of benzene at its m. p., was circulated

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o-*Mercaptoazo-compounds. Part VII.** *Preparation and Debenzylation of* 2 : 2′-*Dibenzylthioazobenzene.*

By A. Burawoy, A. Chaudhuri, and C. E. Vellins.

[Reprint Order No. 6410.]

The action of bromine in glacial acetic acid on 2 : 2′-dibenzylthioazobenzene (I), prepared by reduction of 2-benzylthionitrobenzene with lithium aluminium hydride, is investigated. 2-Benzylthioazobenzene-2′-sulphenyl bromide (II), 2-benzylthioazobenzene-2′-sulphenyl tribromide (III), di-[*o*-(*o*′-bromothiophenylazo)phenyl] disulphide (IV), and azobenzene-2 : 2′-di(sulphenyl bromide) (VI) are isolated and some of their reactions described. The rather unstable 2-benzylthio-2′-mercaptoazobenzene (XV; R = H) and 2 : 2′-dimercaptoazobenzene (XVI; R = H) are formed on reduction of the corresponding disulphide (VII) and polysulphide (XIII) respectively.

The preparation and debenzylation of 2-benzylthioazobenzene have recently been discussed (Part V *). Treatment with 1 and 2 mols. of bromine yields azobenzene-2-sulphenyl bromide and azobenzene-2-sulphenyl tribromide respectively. The former is converted by zinc into di-(*o*-phenylazophenyl) disulphide and by sodium hydroxide into the same disulphide and sodium azobenzene-2-sulphinate, the latter being also obtained by the action of sodium hydroxide on azobenzene-2-sulphenyl tribromide. 2-Mercaptoazobenzene, formed by reduction of the disulphide with sodium sulphide, could not be obtained analytically pure since it is very readily reoxidised to the disulphide, but its existence was established by conversion with methyl sulphate and alkali into 2-methylthioazobenzene and by the preparation of a stable copper complex salt.

We have now investigated the preparation of 2 : 2′-dibenzylthioazobenzene (I) and its debenzylation by means of bromine. The alkaline reduction of *o*-(benzylthio)nitrobenzene with zinc proved unsatisfactory, whilst the reduction with ammonium chloride and zinc in ethanolic solution yields mainly 2 : 2′-dibenzylthioazoxybenzene and, in addition to some *o*-(benzylthio)aniline, only *ca.* 5% of 2 : 2′-dibenzylthioazobenzene. Nystrom and Brown (*J. Amer. Chem. Soc.*, 1948, **70**, 3738) have shown that lithium aluminium hydride is able to reduce nitro-compounds to the corresponding azo-compounds. Applying this method to *o*-(benzylthio)nitrobenzene, we have obtained in ether a mixture of 2 : 2′-dibenzylthioazoxybenzene and -azobenzene, but in benzene–ether solution only the latter in almost quantitative yield.

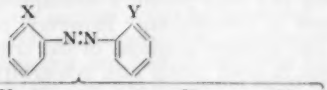
The action of bromine on 2 : 2′-dibenzylthioazobenzene (I) yields various products according to the proportion of bromine and the conditions. The stable 2′-benzylthioazobenzene-2-sulphenyl bromide (II) is formed almost quantitatively by the action of one

* Parts I, IV, V, and VI, *J.*, 1950, 469; 1954, 82, 90, 4481.

mol. of bromine in boiling acetic acid. It is converted into 2′-benzylthioazobenzene-2-sulphenyl tribromide (III) when shaken with an additional mol. of bromine in cold acetic acid. In boiling solution, the tribromide readily dissociates into the sulphenyl bromide (II) and bromine which, at this higher temperature, attacks the second benzylthio-group with the formation of some di-[*o*-(*o*′-bromothiophenylazo)phenyl] disulphide (IV).

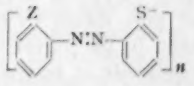
Excess of bromine yields a crystalline product which is probably azobenzene-2 : 2′-di-(sulphenyl tribromide) (V). It is very unstable and, after filtration, quickly loses bromine, leaving as residue the yellow, moderately stable azobenzene-2 : 2′-di(sulphenyl bromide) (VI) which has been characterised by conversion into the corresponding stable water-soluble dichloride and with dimethylaniline into 2 : 2′-di-(*p*-dimethylaminophenylthio)azobenzene (VI; *p*-S·C_6H_4·NMe_2 for SBr). In boiling benzene or acetic acid, the dibromide dissociates into bromine and the stable disulphide (IV), the latter being obtained quantitatively on continuous heating.

2′-Benzylthioazobenzene-2-sulphenyl bromide (II) reacts with zinc in boiling benzene to yield di-[*o*-(*o*′-benzylthiophenylazo)phenyl] disulphide (VII). On addition of sodium

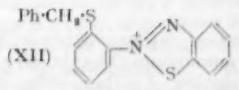


	X	Y
(I)	S·CH_2Ph	S·CH_2Ph
(II)	S·CH_2Ph	SBr
(III)	S·CH_2Ph	SBr_3
(V)	SBr_3	SBr_3
(VI)	SBr	SBr
(VIII)	S·CH_2Ph	SONa

	X	Y
(IX)	S·CH_2Ph	SO_2Na
(X)	S·CH_2Ph	SOMe
(XI)	S·CH_2Ph	SO_2·CH_2Ar
(XV)	S·CH_2Ph	SR
(XVI)	SR	SR



	Z	*n*
(IV)	SBr	2
(VII)	S·CH_2Ph	2
(XIII)	S-	
(XIV)	SONa	2



hydroxide to a solution of the sulphenyl bromide (II) in aqueous ethanol a deep blue colour develops immediately owing to formation of sodium 2′-benzylthioazobenzene-2′-sulphenate (VIII). Although the latter could not be isolated, its existence has been established by immediate treatment of the blue solution with methyl sulphate, whereby *o*-(*o*′-benzylthiophenylazo)phenyl methyl sulphoxide (X) is formed. The blue colour disappears after a few hours, disproportionation taking place with formation of the insoluble disulphide (VII) (93%) and the soluble sodium 2′-benzylthioazobenzene-2-sulphinate (IX) which on acidification yields the crystalline orange acid (67%). On longer stirring, the amount of the sulphinic acid increases at the expense of the disulphide. Undoubtedly,the disulphide linkage is slowly attacked by sodium hydroxide, forming the thiol and the sulphenate, the former being readily reoxidised to the disulphide and the latter again undergoing disproportionation with formation of the disulphide and more sulphinic acid.

2′-Benzylthioazobenzene-2-sulphinic acid is also obtained almost quantitatively by the action of excess of sodium hydroxide on the tribromide (III). As with the parent azobenzene-2-sulphenyl tribromide (Part V, *loc. cit.*), the blue intermediate colour of the sulphenate is not observed, thus supporting structure (III) for the tribromide. The sulphinic acid (as IX) has been characterised as *o*-(*o*′-benzylthiophenylazo)phenyl nitrobenzyl sulphone (XI) and its structure further confirmed by conversion by hydrobromic acid in acetic acid into the sulphenyl bromide (II), a general reaction of aromatic sulphinic acids (cf. Fries, *Ber.*, 1912, **45**, 2965; Fries and Schürmann, *ibid.*, 1914, **47**, 1195; Parts I and V of this series, *locc. cit.*).

Like azobenzene-2-sulphenyl bromide, its 2′-benzylthio-derivative (II) is converted by double decomposition reactions in aqueous ethanol into the corresponding cyanide, thiocyanate, chloride, iodide, and perchlorate. The iodide is less stable than azobenzene-2-sulphenyl iodide and could not be obtained analytically pure. When heated in solution it readily dissociates into the disulphide and iodine. The properties of these sulphenyl derivatives are similar to those of the parent azobenzene-2-sulphenyl derivatives. As

discussed in Part VI (*loc. cit.*), except for the cyanide, they are able to exist as true salts of structure (XII). The quantitative aspect of this problem is being further investigated.

The bisbromothio-disulphide (IV) is converted by zinc in boiling toluene into an orange product which is either the tetrasulphide or the hexasulphide (XIII; $n = 2$ or 3) : low solubility precluded a determination of its molecular weight. Addition of aqueous sodium hydroxide to a suspension of the disulphide (IV) in ethanol results in the immediate formation of a blue solution, probably containing the sodium salt (XIV) of the sulphenic acid disulphide. After 20 hours' stirring the blue colour disappears with formation of the insoluble orange polysulphide (XIII) and a red solution yielding on acidification a mixture from which only a colourless substance moderately soluble in ethanol and crystallising as large needles could be obtained in a pure state. Its analysis agrees with the empirical formula $C_{12}H_8O_3N_2S_2$ and the absence of colour excludes the presence of an azo-group. The structure of this product requires further elucidation.

Reduction of the disulphide (VII) and the polysulphide (XIII) with sodium sulphide in ethanol yields 2-benzylthio-2′-mercaptoazobenzene (XV; R = H) and 2 : 2′-dimercaptoazobenzene (XVI; R = H), which like their parent 2-mercaptoazobenzene could not be obtained pure owing to their ease of reoxidation. However, their existence could be established (i) by conversion of the alkaline solutions of the crude isolated products by methyl sulphate or benzyl chloride in good yields into 2-benzylthio-2′-methylthio- (XV; R = Me) and 2 : 2′-dimethylthio-azobenzene (XVI; R = Me) on the one hand, and 2 : 2′-dibenzylthio-azobenzene (XVI; R = CH_2Ph) on the other, and (ii) by the isolation of copper complex salts of the probable structures (XV; R = $\frac{1}{2}$Cu) and (XVI; R = $\frac{1}{2}$Cu) respectively.

Experimental

Reduction of o-*(Benzylthio)nitrobenzene with Zinc and Ammonium Chloride.*—Zinc dust (10 g.) and ammonium chloride (20 g.) in water (80 c.c.) were added alternately with stirring to a boiling solution of *o*-(benzylthio)nitrobenzene (9 g.) in ethanol (350 c.c.). After refluxing for 4 hr., the hot mixture was filtered. On cooling, almost pure 2 : 2′-*dibenzylthioazoxybenzene* separated (4·95 g., 61%). Crystallisation from ethanol gave yellow needles, m. p. 155—156° (Found : C, 70·3; H, 5·2; N, 6·0. $C_{26}H_{22}ON_2S_2$ requires C, 70·6; H, 5·0; N, 6·4%). Steam-distillation of the ethanolic filtrate yielded *o*-(benzylthio)aniline (0·3 g., 4%), m. p. 43—44° (after crystallisation from light petroleum), identical with an authentic specimen. The zinc residue was extracted with toluene from which 2 : 2′-*dibenzylthioazobenzene* (0·4 g., 5%) was obtained. It is almost insoluble in ethanol and crystallised from toluene as orange needles, m. p. 222—223° (Found : C, 73·4; H, 5·3; N, 6·2. $C_{26}H_{22}N_2S_2$ requires C, 73·2; H, 5·2; N, 6·6%).

Reduction of o-*(Benzylthio)nitrobenzene with Lithium Aluminium Hydride.*—(i) A solution of *o*-(benzylthio)nitrobenzene (10 g.) in dry ether (500 c.c.) was added with stirring to a solution of lithium aluminium hydride (2·75 g.) in dry ether (250 c.c.) at such a rate that the solution was kept gently boiling. After refluxing for 2 hr., the mixture was poured into 10% sulphuric acid (100 c.c.) and ice (500 g.). The precipitate consisting of 2 : 2′-dibenzylthio-azo- and azoxy-benzene was collected. The azoxy-compound (3·5 g., 39%; m. p. 153—154°) was extracted with boiling ethanol, leaving a residue of the slightly impure azo-compound (4·6 g., 53%; m. p. 212—214°). (ii) The experiment was repeated with the exception that *o*-(benzylthio)nitrobenzene (10 g.) in benzene (500 c.c.) was added to the solution of lithium aluminium hydride in ether. Only 2 : 2′-dibenzylthioazobenzene was obtained (8 g., 92%; m. p. 206—210°) which crystallised from toluene as orange needles, m. p. 222—223°, identical with the product obtained in the reduction with zinc and ammonium chloride.

2′-*Benzylthioazobenzene*-2-*sulphenyl Bromide* (II).—2 : 2′-Dibenzylthioazobenzene (8 g.), glacial acetic acid (300 c.c.), and bromine (3 g., 1 mol.) were refluxed for 3 min. On cooling, 2′-*benzylthioazobenzene*-2-*sulphenyl bromide* (5·8 g.) slowly crystallised and was collected. Chloroform-extraction of the filtrate yielded a further 1·2 g. (total, 90%). Crystallisation from benzene gave orange-yellow plates, m. p. 183—184° (Found : C, 54·9; H, 4·0; N, 6·8. $C_{19}H_{15}N_2S_2Br$ requires C, 54·9; H, 3·6; N, 6·8%), almost insoluble in ether and light petroleum, sparingly soluble in water, moderately in ethanol and benzene, and easily in chloroform.

2′-*Benzylthioazobenzene*-2-*sulphenyl Tribromide* (III).—(i) A suspension of 2 : 2′-dibenzylthioazobenzene (1 g.) in acetic acid (100 c.c.) was shaken with bromine (0·75 g., 2 mol.) for 3 days.

The orange-yellow, almost pure *sulphenyl tribromide*, m. p. 99—102°, crystallised (1·15 g., 83%) (Found: C, 39·0; H, 2·6; Br, 40·8. $C_{19}H_{15}N_2S_2Br_3$ requires C, 39·7; H, 2·6; Br, 41·7%). No improvement in purity was effected by crystallisation from acetic acid or benzene, which caused partial dissociation into the monobromide and bromine. (ii) A suspension of 2′-benzylthioazobenzene-2-sulphenyl bromide (1 g.) in glacial acetic acid (100 c.c.) was shaken with bromine (0·4 g., 1 mol.) for 3 days. The precipitate of almost pure crystalline tribromide, m. p. 99—102°, was collected (1·3 g., 94%). (iii) A suspension of the tribromide (1 g.) in acetic acid (50 c.c.) was shaken with bromine (0·63 g., 2 mol.) at room temperature for 2 days. No reaction occurred, the starting material being recovered quantitatively.

Di-[o-(o′-*bromothiophenylazo*)*phenyl*] *Disulphide* (IV).—(i) A suspension of 2 : 2′-dibenzylthioazobenzene (2 g.) in acetic acid (60 c.c.) was refluxed with bromine (1·5 g., 2 mol.) for 3 min. On cooling, a tar separated (1·4 g.). The filtrate was extracted with chloroform and the red tar with benzene, from which solvents 2′-benzylthioazobenzene-2-sulphenyl bromide was obtained (1·2 g., 62%). The solid residue consisted of crude *bisbromothio-disulphide*, which crystallised from chlorobenzene or acetic acid as yellow needles, m. p. 264—265° (0·4 g., 24%) (Found: C, 44·7; H, 2·4; N, 8·7. $C_{24}H_{16}N_4S_4Br_2$ requires C, 44·5; H, 2·5; N, 8·6%). (ii) 2′-Benzylthioazobenzene-2-sulphenyl bromide (1 g.), acetic acid (30 c.c.), and bromine (0·4 g., 1 mol.) were refluxed for 3 min. On cooling, a red tar separated. The mixture was worked up as above. Starting material (0·45 g.) was recovered, and the yield of disulphide was 0·3 g. (70%). (iii) The experiment was repeated, but boiling continued for 1 hour, the corresponding yields then being 0·2 g. and 0·5 g. (79%). (iv) 2′-Benzylthioazobenzene-2-sulphenyl bromide (1 g.), acetic acid (30 c.c.), and bromine (0·8 g., 2 mol.) were refluxed for 3 min. No starting material was recovered and the yield of disulphide was 0·6 g. (77%). (v) No reaction occurred when a suspension of the bisbromothio-disulphide (0·5 g.) in acetic acid (50 c.c.) was shaken with bromine (0·124 g., 1 mol.) for 2 days.

*Azobenzene-*2 : 2′-*di*(*sulphenyl Bromide*) (VI).—(i) A suspension of 2 : 2′-dibenzylthioazobenzene (2 g.) in acetic acid (60 c.c.) was refluxed with bromine (3 g., 4 mol.) for 3 min. On cooling, orange plates, m. p. 134—136°, contaminated with a red tar, separated and were collected. The fuming unstable orange plates, which might be azobenzene-2 : 2′-di(sulphenyl tribromide) (V), quickly lost bromine in air and changed to a more stable yellow product. Rapid crystallisation from acetic acid containing a drop of bromine yielded hydrated *azobenzene-*2 : 2′-*di*(*sulphenyl bromide*), m. p. 199° (Found: C, 33·7; H, 2·3; Br, 38·8. $C_{12}H_8N_2S_2Br_2,H_2O$ requires C, 34·1; H, 2·3; Br, 37·9%), sparingly soluble in water and moderately in ethanol. Crystallisation after prolonged heating either of the original orange plates or of the di(sulphenyl bromide) from chlorobenzene or acetic acid gave pure bisbromothio-disulphide (IV), m. p. 264—265°. (ii) The bisbromothio-disulphide (0·5 g.), acetic acid (50 c.c.), and bromine (0·5 g., 4 mol.) were shaken for 2 days. The filtered red solid changed in air with liberation of bromine into the yellow azobenzene-2 : 2′-di(sulphenyl bromide), m. p. 199° (0·5 g., 80%).

*Azobenzene-*2 : 2′-*di*(*sulphenyl Chloride*).—To pure azobenzene-2 : 2′-di(sulphenyl bromide) (0·5 g.) suspended in acetic acid (100 c.c.) was added concentrated hydrochloric acid (100 c.c.) and the mixture shaken for 6 hr. The resulting solution was diluted with water and extracted with chloroform, which after drying was evaporated to a small volume. On addition of light petroleum *azobenzene-*2 : 2′-*di*(*sulphenyl chloride*) (0·25 g., 63%) separated. It crystallised from chlorobenzene as a pale yellow solid, m. p. 215°, soluble in water and ethanol (Found: C, 45·4; H, 2·5; N, 8·3. $C_{12}H_8N_2S_2Cl_2$ requires C, 45·7; H, 2·5; N, 8·8%).

2′-*Benzylthioazobenzene-*2-*sulphenyl Chloride*.—A solution of 2′-benzylthioazobenzene-2-sulphenyl bromide (0·5 g.) in warm ethanol (65 c.c.) was added to water (250 c.c.) and concentrated hydrochloric acid (20 c.c.), and the whole extracted with chloroform, from which, after evaporation, the *chloride* was obtained (0·35 g., 78%). It crystallised from benzene as orange-yellow needles, m. p. 160—161° (sintering at 96°), containing benzene of crystallisation which could be removed only *in vacuo* at 100° for 5 hr. (Found, after 3 hours' drying at 70° *in vacuo*: C, 64·4; H, 4·6; N, 7·0. $C_{19}H_{15}N_2S_2Cl,\frac{1}{2}C_6H_6$ requires C, 64·5; H, 4·4; N, 6·9%; after drying to constant weight at 100° *in vacuo*: C, 60·9; H, 3·8; loss, 9·5. $C_{19}H_{15}N_2S_2Cl$ requires C, 61·5; H, 4·1; loss, 9·5%).

2′-*Benzylthioazobenzene-*2-*sulphenyl Iodide*.—A solution of the bromide (0·5 g.) in warm ethanol (65 c.c.) was added to an ice-cold solution of potassium iodide (3 g.) in water (200 c.c.). There was immediate deposition of the orange-brown *iodide*, m. p. 190—191°, which was filtered off, washed, and dried (Found: C, 47·3; H, 2·9. $C_{19}H_{15}N_2S_2I$ requires C, 49·3; H, 3·3%). Crystallisation from benzene or slow crystallisation from ethanol yielded pure di-[o-(o′-benzylthiophenylazo)phenyl] disulphide (VII), m. p. 230—231°, described below.

2'-Benzylthioazobenzene-2-sulphenyl Perchlorate.—A solution of 2-benzylthioazobenzene-2-sulphenyl bromide (0·5 g.) in warm ethanol (65 c.c.) was added to an ice-cold solution of sodium perchlorate (3 g.) in water (200 c.c.). The precipitate of almost pure *perchlorate* (0·5 g., 86%) was filtered off. It crystallised from aqueous ethanol as orange needles, m. p. 113—115° (with detonation) (Found : C, 52·5; H, 3·3. $C_{19}H_{15}O_4N_2S_2Cl$ requires C, 52·5; H, 3·5%).

2'-Benzylthioazobenzene-2-sulphenyl Thiocyanate.—A solution of the same bromide (0·5 g.) in warm ethanol (70 c.c.) was added to an ice-cold solution of potassium thiocyanate (2 g.) in water (100 c.c.). The slowly formed precipitate of the *thiocyanate* was collected and washed with water (0·35 g., 78%). It crystallised from benzene as yellow-orange needles, m. p. 106° (Found : C, 61·6; H, 3·8; N, 10·4. $C_{20}H_{15}S_3N_3$ requires C, 61·1; H, 3·8; N, 10·6%).

2'-Benzylthioazobenzene-2-sulphenyl Cyanide (*2-Benzylthio-2'-thiocyanatoazobenzene*).—The above experiment was repeated, but with potassium cyanide in place of potassium thiocyanate. The precipitated *cyanide* (0·49 g., 83%) was filtered off and washed with water. It crystallised from ethanol as orange needles, m. p. 129—130° (Found : C, 66·5; H, 4·0; N, 11·8. $C_{20}H_{15}N_3S_2$ requires C, 66·5; H, 4·0; N, 11·6%).

Action of Zinc on 2'-Benzylthioazobenzene-2-sulphenyl Bromide.—This bromide (1 g.), benzene (100 c.c.), and zinc dust (5 g.) were refluxed for 20 min. The hot solution was filtered and concentrated. On cooling, *di*-[o-(o'-*benzylthiophenylazo*)*phenyl*] *disulphide* separated (0·65 g., 81%). Crystallisation from benzene gave a yellow-orange solid, m. p. 230—231° (Found : C, 67·9; H, 4·6; N, 8·1. $C_{38}H_{30}N_4S_3$ requires C, 68·1; H, 4·5; N, 8·4%).

Action of Sodium Hydroxide on 2'-Benzylthioazobenzene-2-sulphenyl Bromide.—(i) 10% Sodium hydroxide solution (20 c.c.) was added with stirring to a suspension of the bromide (2 g.) in water (100 c.c.) and ethyl alcohol (50 c.c.). A deep blue colour developed which disappeared after 3 hours' stirring, during which di-[o-(o'-benzylthiophenylazo)phenyl] disulphide separated; this was collected (1 g., 93%), and crystallisation from benzene gave a yellow-orange solid, m. p. 230—231°, identical with that described above. Acidification of the filtrate with hydrochloric acid precipitated almost pure *2'-benzylthioazobenzene-2-sulphinic* acid (0·4 g., 67%). It crystallised from aqueous alcohol as orange needles, m. p. 125—126° (Found : C, 61·9; H, 4·5; N, 7·5. $C_{19}H_{16}N_2O_2S_2$ requires C, 61·9; H, 4·4; N, 7·6%). (ii) The experiment was repeated, but stirring continued for 20 hr. The yields then were : disulphide, 0·8 g. (74%); sulphinic acid, 0·7 g. (116%).

Action of Sodium Hydroxide on 2'-Benzylthioazobenzene-2-sulphenyl Tribromide (III).—10% Aqueous sodium hydroxide (30 c.c.) was added to a solution of the tribromide (1 g.) in ethyl alcohol (250 c.c.). An immediate red colour developed. After 6 hr. the red solution was acidified with hydrochloric acid. The precipitate of almost pure 2'-benzylthioazobenzene-2-sulphinic acid was filtered off (0·5 g., 78%). It crystallised from aqueous alcohol as orange needles, m. p. 125—126° not depressed by the product obtained by the action of alkali on 2'-benzylthioazobenzene-2-sulphenyl bromide (see above).

o-o'-*Benzylthiophenylazophenyl* p-*Nitrobenzyl Sulphone* (XI).—*p*-Nitrobenzyl bromide (0·6 g.), 2'-benzylthioazobenzene-2-sulphinic acid (0·5 g.), sodium hydroxide (0·07 g.), and ethanol (75 c.c.) were refluxed for 7 hr. On cooling, the *sulphone* crystallised (0·4 g., 58%). Recrystallisation from ethanol gave yellow-orange needles, m. p. 210—212° (Found : C, 62·0; H, 4·2; S, 12·4. $C_{26}H_{21}O_4N_3S_2$ requires C, 61·5; H, 4·1; S, 12·7%).

Action of Hydrobromic acid on 2'-Benzylthioazobenzene-2-Sulphinic Acid (as IX).—The sulphinic acid (0·5 g.), acetic acid (30 c.c.), and 48% hydrobromic acid (10 c.c.) were refluxed for 5 min. After addition of water, 2'-benzylthioazobenzene-2-sulphenyl bromide was extracted with chloroform (0·45 g., 80%; m. p. 180—182° before crystallisation).

o-o'-*Benzylthiophenylazophenyl Methyl Sulphoxide* (X).—2'-Benzylthioazobenzene-2-sulphenyl bromide (0·5 g.), 10% aqueous sodium hydroxide (20 c.c.), and ethanol (50 c.c.) were shaken for 5 min. A deep blue colour developed. Methyl sulphate (3 c.c.) was added, and shaking continued for 30 min. The precipitated *sulphoxide* (0·3 g., 68%) was filtered off and crystallised from ethanol as yellow-orange needles, m. p. 194—195° (sintering at 186°) (Found : C, 66·2; H, 5·0. $C_{20}H_{18}ON_2S_2$ requires C, 65·6; H, 4·9%).

2-Benzylthio-2'-mercaptoazobenzene (XV; R = H).—(i) Sodium sulphide nonahydrate (2 g.) and sodium hydroxide (2 g.) in water (20 c.c.) were added to a solution of di-[o-(o'-benzylthiophenylazo)phenyl] disulphide (0·3 g.) in benzene (150 c.c.) and ethanol (150 c.c.), and the mixture refluxed for 20 min. The resultant clear red solution was cooled and poured into a separatory funnel containing ice-cold water (100 c.c.). The red aqueous layer was quickly separated from the almost colourless benzene layer, saturated with salt, and acidified with hydrochloric acid. The precipitated yellow 2-benzylthio-2'-mercaptoazobenzene (0·2 g., 66%) was quickly filtered

off, washed with water, and dried *in vacuo*. Before drying it melted at 180—184°, and after drying at 204—210°, being readily reoxidised to the original disulphide. When freshly prepared, the thiol was soluble in light petroleum or alcohol and gave a red solution in alcoholic sodium hydroxide. Attempts to recrystallise the crude thiol resulted in formation of the disulphide, m. p. 230—231°. (ii) The experiment was repeated, but the red aqueous layer after separation from benzene was shaken with methyl sulphate (2 c.c.) for 1 hr. Almost pure *2-benzylthio-2′-methylthioazobenzene* separated (0·25 g., 79%). Crystallisation from light petroleum (b. p. 80—100°) gave red-orange needles, m. p. 137—138° (Found: C, 68·8; H, 5·1; S, 17·8. $C_{20}H_{18}N_2S_2$ requires C, 68·6; H, 5·1; S, 18·3%). (iii) Crude, freshly prepared 2-benzylthio-2′-mercaptoazobenzene (0·25 g.) was shaken with ethanol (50 c.c.) and 10% aqueous sodium hydroxide (5 c.c.) for 3 min. The red solution was filtered from some disulphide (0·1 g.) and shaken with methyl sulphate (0·3 c.c.) for 1 hr. The precipitated 2-benzylthio-2′-methylthioazobenzene was collected (0·1 g., 39%). It crystallised from light petroleum (b. p. 60—80°) as orange needles, m. p. 137—138°, undepressed by the product obtained as above.

Copper Complex Salt of 2-Benzylthio-2′-mercaptoazobenzene (XV; R = ½Cu).—Di-[*o*-(*o′*-benzylthiophenylazo)phenyl] disulphide (0·3 g.) was reduced as described above. The red solution was poured into a separatory funnel containing ice-water and benzene. On acidification with hydrochloric acid, the thiol passed into the benzene layer which was washed with water. 10% Aqueous sodium hydroxide (50 c.c.) and salt (10 g.) were added, and the mixture was shaken for 10 min. The precipitated sodium derivative of 2-benzylthio-2′-mercaptoazobenzene (0·15 g.) was filtered off and redissolved in ethanol (50 c.c.). A dark green *copper complex* separated on addition of a solution of copper sulphate (1 g.) in water (150 c.c.); it was filtered off after 20 hr., dried, and purified by precipitation from solution in chloroform by light petroleum (0·1 g.; m. p. 310—312°) (Found: C, 61·0; H, 4·4; N, 7·3; Cu, 8·4. $C_{28}H_{30}N_4S_4Cu,H_2O$ requires C, 60·6; H, 4·3; N, 7·5; Cu, 8·5%).

2 : 2′-Di-(p-dimethylaminophenylthio)azobenzene.—Dimethylaniline (1·5 c.c.) was added to a suspension of azobenzene-2 : 2′-di(sulphenyl bromide) (0·5 g.) in acetic acid (10 c.c.), and the mixture refluxed for 15 min. There was an immediate reaction, and the red *2 : 2′-di-(p-dimethylaminophenylthio)azobenzene* separated. Crystallisation from chlorobenzene yielded a red powder, m. p. 283—285° (Found: C, 68·7; H, 5·6; N, 11·2. $C_{28}H_{28}N_4S_2$ requires C, 69·3; H, 5·8; N, 11·6%).

Action of Zinc on Di-[o-(o′-bromothiophenylazo)phenyl] Disulphide (IV).—The disulphide (0·3 g.), zinc dust (4 g.), and toluene (200 c.c.) were refluxed for 20 min. The mixture was filtered hot and allowed to cool. A yellow precipitate of the *polysulphide* (XIII; $n \geqslant 2$) separated slowly and was collected (0·15 g., 67%; m. p. 266—268°). It is almost insoluble in organic solvents, but crystallised from nitrobenzene–chlorobenzene as an orange powder, m. p. 266—268° (sintering below 200°) [Found: C, 59·7; H, 3·1; N, 11·3. $(C_{12}H_8N_2S_3)n$ requires C, 59·0; H, 3·3; N, 11·5%].

Action of Sodium Hydroxide on the Bisbromothio-disulphide (IV).—Sodium hydroxide (5 g.) in water (200 c.c.) was added to a suspension of the disulphide (IV) (2·7 g.) in ethanol (120 c.c.). A blue colour developed, but disappeared after 20 hours' stirring. A yellow precipitate was collected (1·3 g., 95%). It crystallised from nitrobenzene–chlorobenzene as an orange powder, m. p. 266—268°, identical with the polysulphide described above. Acidification of the filtrate with hydrochloric acid yielded a yellow precipitate (0·6 g.) which on crystallisation from ethanol gave white needles, m. p. 182—183° (becoming red before melting). The *substance* is sparingly soluble in ethanol and dissolves in aqueous sodium hydroxide with an orange-yellow colour (Found: C, 49·7; H, 3·1; N, 9·4. $C_{12}H_8O_3N_2S_2$ requires C, 49·3; H, 2·8; N, 9·6%). The ethanolic mother-liquors contain an easily soluble yellow acid which could not be obtained pure.

2 : 2′-Dimercaptoazobenzene (XVI; R = H).—(i) A solution of sodium sulphide nonahydrate (1 g.) in 5% aqueous sodium hydroxide (20 c.c.) was added to a suspension of the polysulphide (XIII) (0·3 g.) in ethanol (20 c.c.), and the mixture refluxed for 3 min. The resultant clear red solution was cooled, saturated with salt, and acidified with hydrochloric acid. The precipitate of the yellow crude 2 : 2′-dimercaptoazobenzene was filtered off and dried (0·2 g., 67%). Attempts to crystallise it failed; *e.g.*, heating it with ethanol yielded the insoluble polysulphide (XIII), m. p. 266—268°. (ii) The experiment was repeated, but the clear red solution was shaken with benzyl chloride (1 c.c.) for 1 hr. The precipitate of almost pure 2 : 2′-dibenzylthioazobenzene was collected (0·37 g., 67%); m. p. 222—223°, not depressed by an authentic sample. (iii) The experiment was repeated, but benzyl chloride was replaced by methyl sulphate (1 c.c.). The precipitate of almost pure 2 : 2′-dimethylthioazobenzene (0·3 g., 89%) crystallised from ethanol as orange needles, m. p. 154—155° (Brand, *Ber.*, 1909, **42**, 3463, gives 154—155°).

(iv) A filtered solution of crude, freshly prepared, dried 2 : 2′-dimercaptoazobenzene (0·2 g.) in ethanol (20 c.c.) and 10% aqueous sodium hydroxide (8 c.c.) was shaken for 20 min. with methyl sulphate (0·8 c.c.). After addition of water, the precipitate of 2 : 2′-dimethylthioazobenzene was filtered off (0·1 g., 56%). It crystallised from ethanol as orange needles, m. p. 154—155°. (v) The experiment was repeated, but methyl sulphate was replaced by benzyl chloride (0·8 c.c.). 2 : 2′-Dibenzylthioazobenzene (0·16 g., 43%) was obtained, having m. p. 222—223° after crystallisation from toluene, not depressed by an authentic sample.

Copper Complex Salt of 2 : 2′-Dimercaptoazobenzene (XVI; R = ½Cu).—A solution of copper sulphate (2 g.) in 1% sulphuric acid (150 c.c.) was added to a filtered solution of freshly prepared, crude 2 : 2′-dimercaptoazobenzene (0·3 g.) in ethanol (50 c.c.) and 10% aqueous sodium hydroxide (10 c.c.). After 24 hr., the black precipitate was filtered off, washed with water and then ethanol, and dried (0·15 g., 40%). The complex *salt* did not melt below 400°, was insoluble in all solvents, and could not be further purified (Found: S, 19·3; Cu, 19·9. $C_{24}H_{16}N_4S_4Cu_2$ requires S, 20·8; Cu, 20·6%).

This investigation has been carried out with the help of a Maintenance Allowance from the Department of Scientific and Industrial Research (to C. E. V.) which is gratefully acknowledged.

College of Technology, University of Manchester. [*Received, May 10th*, 1955.]

The Preparation of Active Solids by Thermal Decomposition. Part VII. The Calcination of* (a) *Ion-free and* (b) *Sulphate-contaminated, Precipitated Alumina Hydrates.*

By S. J. Gregg and K. H. Wheatley.

[Reprint Order No. 6434.]

The effect of sulphate ions on the activation and sintering of precipitated hydrated alumina is somewhat similar to that already reported for precipitated magnesium hydroxide (Part VI*). The influence appears to be indirect rather than direct, in that the part played by the flocculating ions during precipitation and washing of the starting material determines the texture of the solid and thus the behaviour of the solid on heating.

Two batches of alumina hydrate have been prepared, the first by hydrolysis of aluminium ethoxide so as to be virtually free from ionic impurity, and the second by precipitation from aluminium sulphate solution so that it would be contaminated with sulphate ions. A sample of each was first subjected to thermogravimetric analysis, and separate samples from each batch were then heated for 5 hours each at a fixed temperature, and a number of properties of the cooled product (specific surface, density, and lattice structure) were determined. The distinct difference found between the two series of products emphasises the important part played by ionic impurity in determining the properties of "active" oxides.

Experimental

Materials.—The first batch of alumina hydrate (Batch I) was prepared by the hydrolysis of aluminium ethoxide which had been obtained as a greyish powder by refluxing 27 parts of aluminium filings, 0·20 part of mercuric chloride, and several crystals of iodine with 276 parts of absolute alcohol; the excess of alcohol was removed by distillation on an oil-bath, and the residue rapidly distilled *in vacuo* through an air condenser, the pure ethoxide distilling over. A 3% solution of the ethoxide in alcohol was hydrolysed by dropping it into a large quantity of carbon dioxide-free water. The precipitate of hydrated alumina which was formed was washed by decantation, filtered off, and then "dried" by exposure to the atmosphere.

The second batch (Batch II) was prepared by precipitating aluminium sulphate solution with ammonia solution. The precipitation was carried out in three glass tanks each of about 15 l. capacity, and each contained 5 l. of water to which 2 l. of N-aluminium sulphate had been added; 2·5 l. of N-ammonia solution were then run into each with constant stirring, and after

* Part VI, *J.*, 1955, 51.

the precipitate had settled the supernatant liquid was siphoned off. The sludge was then washed several times with large quantities of distilled water, filtered at the pump, and "dried" as before by exposure to the atmosphere.

Procedure.—To throw light on the chemical composition of the two starting materials, they were both subjected to thermogravimetric analysis: each was placed in a crucible on a thermal balance and the temperature of the furnace was raised at the uniform rate of 3°/min., frequent readings of the weight being taken till the temperature reached 600° or so (cf. Gregg and Stephens, *J.*, 1953, 3951). For expulsion of the remainder of the volatile material in order to find the weight of the anhydrous sample, it would be necessary to raise the temperature to 1250°, but this was unattainable with the furnace. Accordingly, the temperature was raised only to 980° and was kept there till no further change in weight occurred. The correction corresponding to the further loss in weight which would have occurred on raising the temperature from 980° to 1250° was then determined in a further experiment in which a separate sample was calcined at 980° till no further loss in weight occurred, and was then heated for a further 6 hr. in a high-temperature furnace at 1250° and reweighed.

For preparation of the calcination series, separate samples (about 9 g.) from each batch were then heated for 5 hr. in a furnace each at a different fixed temperature $T°$ lying between 200° and 1100°. The following properties of the cooled product were then determined: (*a*) sorption of nitrogen at −183° to find the specific surface (Gregg and Stephens, *loc. cit.*); (*b*) the density in carbon tetrachloride (*J. Phys. Chem.*, 1952, **56**, 388); (*c*) the *X*-radiogram (kindly determined by Drs. H. Lipson and C. A. Taylor). The content of volatile matter had to be obtained indirectly: a separate sample was calcined as above, and the weight of the anhydrous material was determined exactly as in the thermogravimetric experiment.

Results and Discussion

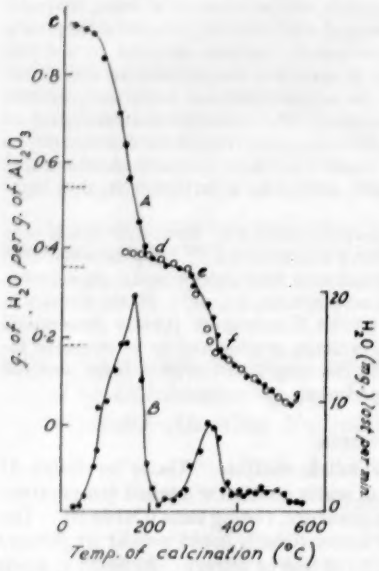
We deal first with the results of the thermogravimetric analysis. Those for Batch II are the simpler and are given in Fig. 2 both as a plot of water content w against temperature (Curve *A*) and as the derived curve $\Delta w/\Delta t$ against temperature, t being time (Curve *B*). The loss below 300° is most probably due to adsorbed water (which could persist at *furnace* temperatures much above 100° owing to the finite rate of loss of water). At point *c*, when the temperature is *ca.* 300° and the composition is $Al_2O_3,3H_2O$, the rate of loss greatly increases and the weight falls continuously till the composition is close to $Al_2O_3,0{\cdot}5H_2O$ (point *d*); and, although this could represent a mixture in equal proportions of Al_2O_3 and AlO·OH, the alternative possibility that the "water" is chemisorbed on a bulk material which is anhydrous, cannot be ruled out; for the water content, though so large, is still only of the order required to cover the surface of the micelles with chemisorbed OH groups. [Though the specific surface of the material at *d* was not determined directly, the specific surface of a material of corresponding composition in the calcination series (*viz.*, that at 300°, cf. Fig. 3) was about 400 m.^{2}/g.; and one molecule of water being assumed to cover 15 Å^2 of surface, the "water" content corresponding to $Al_2O_3,0{\cdot}5H_2O$ would cover 450 m.^{2}/g. of solid.]

Whatever the composition at *d*, however, it is clear that the original material had the composition $Al_2O_3,3H_2O$, and this is confirmed by the *X*-ray analysis which shows the presence of bayerite (α-$Al_2O_3,3H_2O$) only.

The results for Batch I are more complicated. As will be seen from Fig. 1, the initial water content is in excess of that required for the trihydrate, and there is no break in the curve at the composition $Al_2O_3,3H_2O$. On the other hand, there is a distinct break in the region of $Al_2O_3,2{\cdot}2H_2O$ (*d*), the rate of loss of water becoming markedly slower until the composition is close to $Al_2O_3,2{\cdot}0H_2O$ (*e*). It is interesting and satisfactory that the curve *defg* was closely reproduced with a second sample.

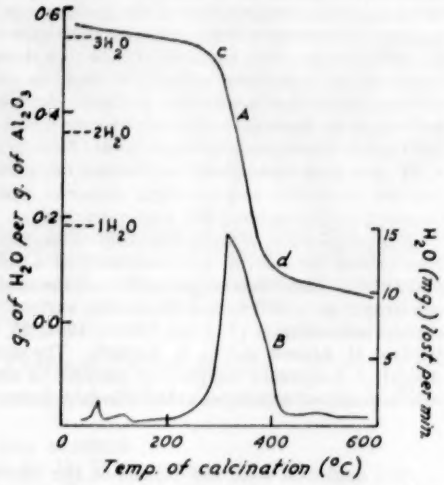
The loss over the range *cd* would seem to represent adsorbed water; for a sample when outgassed for several hours at 25° (a procedure which should remove adsorbed water only) showed a loss in weight corresponding closely to *cd*; and when it was then subjected to thermogravimetric analysis it closely followed the curve obtained with the non-outgassed material (Fig. 1, circles). The fact that the composition at *e* is so close to $Al_2O_3,2H_2O$ might seem to imply that the starting material at *c* consisted of a dihydrate along with adsorbed water; this, however, is not only unlikely on general grounds, but the alternative,

FIG. 1. *Thermogravimetric analysis of Batch I of alumina hydrate (ion-free, from aluminium ethoxide), for a rate of rise of temperature of 3° per minute.*



Curve *A*, The water content is plotted against temperature of calcination.
Curve *B*, The rate of loss of water is plotted against temperature of calcination.

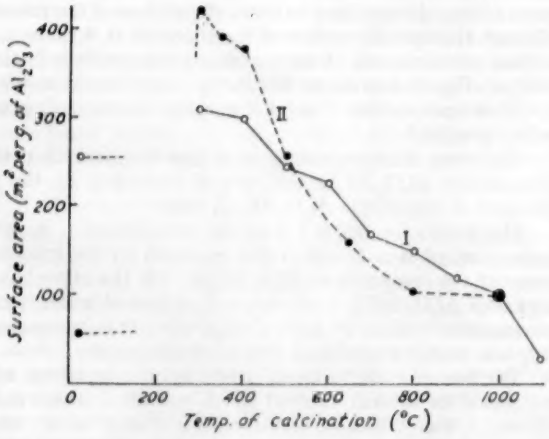
FIG. 2. *Thermogravimetric analysis of Batch II of alumina hydrate (ion-contaminated, from aluminium sulphate) for a rate of rise of temperature of 3° per minute.*



Curve *A*, The water content is plotted against temperature of calcination.
Curve *B*, The rate of loss of water is plotted against temperature of calcination.

FIG. 3. *Surface area (expressed per g. of Al_2O_3) of the product obtained by calcining alumina hydrate for 5 hours at temperature T°, plotted against T°.*

Curve I, for Batch I (ion-free).
Curve II, for Batch II (ion-contaminated).



and more plausible, view that it comprises an equimolecular mixture of the tri- and the monohydrate is supported by the *X*-ray data on the starting material, which showed lines corresponding to bayerite (α-$Al_2O_3,3H_2O$) and boehmite (γ-AlO·OH) only.

For each batch the curve of specific surface against temperature of calcination (Fig. 3) shows the characteristic increase in specific surface consequent on thermal decomposition followed by a decrease due to sintering (cf. Part I, *J.*, 1953, 3940). There is the marked difference between the two batches, however, inasmuch as with Batch I the surface (calc. per g. of Al_2O_3) increases relatively slightly when the water is driven off, whereas with Batch II the increase is at least seven-fold; also the fall due to sintering is considerably sharper both absolutely and relatively for Batch II till 800° is reached. The presence of a (quite small) percentage of sulphate ions (see Table) thus exercises a marked effect on the rate of sintering. This percentage is far too small to form a complete monolayer on the surface, and indeed is only enough to cover a little more than 1% of it; it would seem unlikely therefore that the ions are able to exert a *direct* influence on sintering, *e.g.*, by acting as a film which becomes mobile at elevated temperatures and so acts as a cement. More probably the ions dictate the structure of the starting material through their presence when it is being precipitated and washed. The starting material of Batch II is essentially a flocculated sol; the individual sol particles must have been built up from Al^{+++} and OH^- ions, giving a hydrated oxide, the lattice of which is no doubt very imperfect. The individual sol particles would be temporarily stabilised by an excess of Al^{+++} ions with SO_4^{--} and OH^- as counter-ions, and would then, as sufficient SO_4^{--} ions arrived by diffusion into the

*Certain properties of the products from calcining hydrated alumina for 5 hours at temperature T°.**

T°	S	Δw	ρ	SO_4	X-Ray pattern	T°	S	Δw	ρ	SO_4	X-Ray pattern
		Batch I (ion-free)						Batch II (ion-contaminated)			
15	—	91·1	—	—	*ca.* 50% ba, 50% bo	25	36	56·2	2·43	0·32	mostly ba
						200	46	—	2·46	—	—
25	181	40·3†	2·58	—	—	300	386	9·26	3·15	—	η
300	269	15·3	2·98	—	70% bo, 30% γ-type	350	359	9·2	3·27	0·32	—
						400	353	6·0	3·28	—	γ
400	281	6·9	3·18	—	γ or η	500	246	3·7	3·41	—	γ-type
500	235	3·5	3·37	—	γ	650	154	1·5	3·49	0·32	γ
600	220	1·9	3·41	—	γ	800	103	0·8	3·58	0·24	γ-type; δ?
700	164	1·4	3·48	—	γ	1000	99	0·4	3·55	0·19	γ-type; θ
800	146	1·2	3·52	—	γ	1300	—	—	3·98	—	—
900	117	0·8	3·51	—	γ-type; θ?						
1000	98	0·6	3·54	—	γ-type; θ?			Cf. Corundum 3·98—4·01			
1100	27	—	3·56	—	α						

* S = specific surface per g. of solid, measured by N_2-sorption.
ρ = apparent density in carbon tetrachloride.
Δw = loss in weight at 1250° (g. per 100 g. of Al_2O_3).
SO_4 = sulphate content (g. per 100 g. of Al_2O_3).
ba = bayerite, α-$Al(OH)_3$; bo = boehmite, γ-AlO·OH.
α, γ, δ, η, θ are α-Al_2O_3, γ-Al_2O_3, etc.
† On prolonged evacuation.

electrical double layer, undergo flocculation. A compact precipitate would thus result, each grain of which would consist of an aggregate of the original sol particles, each of which in turn would carry its layer of SO_4^{--} ions; thus the grains of precipitate would have SO_4^{--} ions included within them and not merely located on the outer surface. By contrast, the starting material of Batch I, being formed by hydrolysis of the ethoxide, was precipitated in the virtual absence of ions; one pictures a polymerisation of molecular units of $Al(OH)(OEt)_2$, $Al(OH)_2(OEt)$, and $Al(OH)_3$, probably occurring through hydrogen bonds, producing a solid with so low a degree of order as to be almost amorphous, and occluding a considerable amount of water. The *X*-ray examination (cf. Table), however, showed the solid to be an approximately equimolecular mixture of bayerite and boehmite; and this probably represents a secondary stage resulting from the recrystallisation at room temperature of the amorphous mass into a mixture of micelles of the two products with the elimination of much water and an increase in density. The consequent considerable

shrinkage of the solid would ensure that the component micelles would be in relatively loose contact, the bridges between neighbours being relatively few and weak; the specific surface would thus be large.

With both batches the thermal decomposition gives a product of increased density, and the resultant shrinkage would tend to weaken intermicellar contacts and to reduce their number; nevertheless, the higher degree of compactness of the starting material of Batch II should still persist in the product of calcination also, and so should give a greater tendency to sintering, as is actually found.

The process of crystallisation postulated for Batch I represents an activation of the first of the types discussed in Part I (*loc. cit.*), but occurring at room temperature. The unusually high magnitude of its specific surface shows that the micellar size of the starting material is small, a conclusion confirmed by the considerable degree of line-broadening in the *X*-ray photographs. This helps to explain why the specific surface of this batch increases relatively so little on decomposition: the micelles are so small that there would be a very small probability of a second nucleus in a given micelle being able to grow appreciably before the first nucleus had expanded to include the whole of the micelle.

A number of lattice changes of a minor nature occur when hydrated aluminas are heated over the range 400—900° or so (cf. Day and Hill, *J. Phys. Chem.*, **1953**, **57**, 846). The general tendency of these (the occurrence of which in the present Series is supported by the *X*-ray evidence) would be, as already suggested in Part I, to produce further new surfaces and so to counteract sintering. This could happen by slight changes in density which would introduce strains in joints as yet rather weak and of small cross-section, and also because of imperfect alignment of lattices of contiguous micelles near joints; the latter effect would be intensified where one of the micelles had undergone rearrangement and its neighbour had not.

It will be noted that with Batch II the sintering becomes slower between 600° and 800°, and between 800° and 1000° the fall in specific surface almost ceases. The reason is not clear, but it is interesting and perhaps significant that the sulphate content of this batch first shows a decrease at 800° (Table); and since, as already argued, the SO_4^{--} ions are located on the *surface* of the original sol particles but *within* the grains of the precipitate itself, it may be inferred that these ions first become mobile at this temperature and so can move to the exterior of the grains of the precipitate and there volatilise. Such migration would disturb the junctions, already imperfect, between the sol particles, and so could lead to an increase in surface sufficient to counterbalance the reduction elsewhere due to the normal sintering process. It is unfortunate that no measurement of specific surface for Batch I was made for samples above 1000°, for it would be interesting to know whether an increase in sintering again appears corresponding to that found with Batch I.

The sudden fall in area between 1000° and 1100° with Batch II is associated with the fact that the Tammann temperature (*Z. anorg. Chem.*, **1928**, **176**, 46) of aluminium oxide lies near 1000°, so that one would expect an acceleration in the rate of sintering to commence at this temperature. It seems that this acceleration can more than compensate for the increase in area that might be expected (cf. Part I) to result from the conversion of γ- into α-alumina which occurs between these two temperatures (Table).

We are grateful to Drs. H. Lipson and C. A. Taylor, of Manchester College of Technology, for kindly undertaking the *X*-ray examination of the starting material and the calcined specimens. One of us (K. W.) acknowledges receipt of a Further Education and Training Grant from the Ministry of Education.

WASHINGTON SINGER LABORATORIES,
UNIVERSITY COLLEGE, EXETER.

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Preparation and Structure of Synthetic Hexose Polymers.

By C. R. Ricketts and C. E. Rowe.

[Reprint Order No. 6499.]

A polyglucose can be prepared by deliquescence of glucose crystals over concentrated hydrochloric acid (Ricketts, *J.*, 1954, 4031) or more conveniently by the action of dry gaseous hydrogen chloride on glucose monohydrate. The infrared absorption spectrum resembles that of unbranched dextran and indicates the presence of α-1 : 6-linkages. This was confirmed by paper chromatography and ionophoresis in borate buffer of polyglucose hydrolysates and by the isolation of *iso*maltose as its crystalline octa-acetate. Ionophoresis applied to the polymerisation mixture showed the presence of maltose as well as *iso*maltose, so that α-1 : 4-linkages probably occur in the polyglucose. Polymers have been prepared from other sugars. The polymer from maltose closely resembles polyglucose, suggesting that an equilibrium of all available glucosyl groups contributes to the polymerisation and that appreciable amounts of intact disaccharide are not incorporated into the polymer.

The action of hydrochloric acid on glucose yields a mixture containing disaccharides, higher saccharides, lævoglucosan, and various decomposition products. Choosing conditions giving the maximum yield of disaccharides, so as to reveal the relative proportions of each type of linkage, Thompson, Anno, Wolfrom, and Inatome (*J. Amer. Chem. Soc.*, 1954, **76**, 1309) found *iso*maltose and gentiobiose to be the major products, thereby confirming the work of earlier investigators. Cellobiose and maltose were formed in moderate amounts, so was lævoglucosan. Small amounts of sophorose and trehalose were found. Neither laminaribiose nor nigerose was detected. Thus it appears that the principal types of linkage to be expected in polymers formed from glucose under the catalytic influence of hydrochloric acid are the 1 : 6- and 1 : 4-linkages in α- and β-forms. The possibility that other linkages and anhydro-rings occur in polyglucose cannot be discounted.

The kinetics of the reaction of glucose in hydrochloric acid solution have been investigated several times but in connection with the experiments described in this paper Moelwyn-Hughes's observation (*Trans. Faraday Soc.*, 1928, **24**, 321) that the rate of reaction increases with glucose concentration is significant. Experimental evidence indicated that the reaction was of the pseudo-unimolecular type.

Myrbäck, Hammarstrand, and Gelinder (*Arkiv Kemi*, 1950, **1**, 235) isolated tetrasaccharides containing 1 : 6- and other types of linkage from a solution of glucose in hydrochloric acid. Pacsu and Mora (*J. Amer. Chem. Soc.*, 1950, **72**, 1045) obtained saccharides consisting of about 40 glucose units by evaporation of a solution of glucose in hydrochloric acid to dryness. During the latter stages of this evaporation the molecules may be pictured as being brought closer together in the presence of acid, bonds being formed between them. An alternative means of achieving the conditions of polymerisation was reported in a preliminary communication (Ricketts, *J.*, 1954, 4031). Crystalline anhydrous glucose was allowed to deliquesce in an atmosphere containing water vapour and hydrochloric acid. Under these conditions the molecules, which are as close together as they can be in the crystal, move further apart and pass through the optimum distance for bond formation while under the catalytic influence of acid. A saccharide containing about 20 glucose units and having predominantly 1 : 6-linkages was obtained in 17% yield. The investigation has now been extended to other sugars and a more satisfactory method of carrying out the reaction has been found.

Crystalline glucose monohydrate was found to absorb dry gaseous hydrogen chloride rapidly. By starting with glucose monohydrate the initial water content was defined. The reaction was conveniently carried out in a rotary mixer. Dry hydrogen chloride was passed into about 100 g. of glucose monohydrate, the crystalline powder forming a plastic mass in about 30 minutes. Polymerisation then continued without further addition of hydrogen chloride. Preliminary experiments showed that the maximum degree of

polymerisation was reached in between 1 and 5 days and the latter time was adopted for preparative purposes. The total yield of soluble non-dialysable material was about 45%. The Table shows the properties of two typical polyglucose preparations, P 2 and P 3.

*Properties of hexose polymers.**

	Yield				
	g.	%	$[\alpha]_D^{20}$	$[\eta]$	Reducing value
Polyglucose (P 2)	26·6	32·5	+111° (+52·7°)	0·035	18·4
Polyglucose (P 3)	24·6	30·0	+107 (+52·7)	0·032	16·9
Polyglucose (P)	—	—	+125 (+52·7)	0·033	19·7
Polygalactose	2·8	6·3	+168 (+80·2)	0·032	24·9
Polymaltose	16·0	36·1	+133 (+137)	0·036	20·1
Polylactose	9·9	21·1	+140 (+55·4)	0·034	29·7
Polyglucose-galactose	7·3	21·7	+139	0·036	38·2

* Mutarotation equilibrium values for the original sugar are shown in parentheses. Yields are corrected for moisture content as determined by heating at 100°/0·1 mm. to const. wt. The reciprocal of the reducing value is the reducing power relative to glucose (Shaffer and Hartman, *J. Biol. Chem.*, 1921, **45**, 377).

The products from five such polymerisations were combined and fractionally precipitated from ethanol–water to eliminate short-chain saccharides. The polyglucose (P) so obtained had a somewhat higher optical rotation than the other samples, see Table. The infrared spectrum of polyglucose (P) showed absorption of type 2*a* at 834 cm.$^{-1}$ (Barker, Bourne, Stacey, Whiffen, *J.*, 1954, 171) and no absorption of type 2*b* (890 ± 5 cm.$^{-1}$), from which it was concluded that the links between glucose units were of the α-form. The absorptions of type 1 at 914 cm.$^{-1}$ and type 3 at 760 cm.$^{-1}$ showed that the links involved positions (1) and (6) of the pyranose ring. No 1 : 3-links were detected, there being no absorption maximum at 793 ± 3 cm.$^{-1}$; also no absorption maxima at *ca.* 800 cm.$^{-1}$ associated with furanose rings or 3 : 6-anhydroglucopyranose derivatives were detected. The spectrum was very similar to that of a dextran containing no 1 : 3-linkages.

Polyglucose (P) yielded on oxidation with sodium metaperiodate, 0·72 mole of formic acid per anhydroglucose unit. The interpretation of this result is difficult since the reducing end-group yields several mols. of formic acid, necessitating a large correction for a polymer with relatively short chain-length. The yield of formic acid is less than the theoretical, one mol. for a chain with 1 : 6-links only, by 0·28 mol. Therefore it seems reasonable to assume that at least 28% of the glucose residues are involved in linkages other than the 1 : 6-link. Such linkages may occur at a branching point, in the main chain, or in an anhydro-ring.

Partial hydrolysis of polyglucose in acid, followed by paper chromatography of the de-salted hydrolysate, showed spots at R_G values corresponding to glucose, *iso*maltose, *iso*maltotriose, and *iso*maltotetraose. Dextran hydrolysates, prepared in the same way, were used as controls on the chromatogram. A control experiment showed that under the conditions of hydrolysis only a trace of disaccharide and no higher saccharides were formed from glucose. Some of the higher saccharides from dextran were clearly defined on the chromatograms but the corresponding higher saccharides from polyglucose could not be resolved in repeated attempts. Measurements of electrical conductivity showed that the solutions had been adequately de-salted. This lack of chromatographic resolution may be interpreted as an indication that in the higher saccharides there is an increasing complexity due to the permutation of several types of linkage. Such complexity is necessarily absent from the lower saccharides in a polyglucose hydrolysate and does not arise to the same extent in natural polysaccharides on account of the repeating patterns formed by enzymes.

To obtain supporting evidence the hydrolysis was repeated on a larger scale and the products were separated on a charcoal column (Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 607). Glucose, characterised as the β-penta-acetate, and *iso*maltose, characterised as the crystalline octa-acetate, were isolated. A third fraction was obtained which on paper chromatography showed spots corresponding to *iso*maltotriose and *iso*maltotetraose. Hence blocks of four consecutive 1 : 6-linked glucose units occur in polyglucose.

Information about other types of linkage likely to be present in polyglucose was obtained by subjecting the products of incomplete polymerisation to separation on a charcoal column. On elution with 8% v/v ethanol and freeze-drying a white solid was obtained. Paper chromatography showed a spot with an R_F value identical with that of glucose and a second spot with an R_F value close to that of *iso*maltose. Electrophoresis of the same material in borate buffer showed four spots with M_G values corresponding to glucose, gentiobiose, *iso*maltose, and maltose. Thus, by examination of the products of incomplete polymerisation, the presence of linkages so sensitive to acid hydrolysis that they escaped detection in hydrolysates was revealed. For instance, maltose is hydrolysed four times as rapidly as *iso*maltose (Wolfrom, Lassettre, and O'Neil, *J. Amer. Chem. Soc.*, 1951, **73**, 595).

No polymeric material could be obtained from xylose, fructose, or sucrose on account of the rapid decomposition of pentoses and ketoses under strongly acidic conditions.

Extension of the investigation to disaccharides presents interesting possibilities since the action of hydrochloric acid could lead to incorporation of the intact disaccharide into the polymer or to hydrolysis of the disaccharide to an equilibrium mixture in which all available glycosyl groups participate.

The polymer from maltose was compared with polyglucose. The optical rotation and chain length of polymaltose were slightly greater than the corresponding values for polyglucose as shown in the Table. Paper chromatography of polymaltose hydrolysates showed spots with R_F values corresponding to *iso*maltose and *iso*maltotriose. Oxidation with sodium metaperiodate yielded 0·71 mole of formic acid per anhydroglucose unit, very close to the yield obtained from polyglucose under the same conditions. A lower value would be expected if polymaltose contained more 1 : 4-linkages than polyglucose. The infrared spectrum of polymaltose showed absorption of type 2*a* at 837 cm.$^{-1}$ associated with α-glucopyranose links. Absorption of type 1 at 918 cm.$^{-1}$ showed that long sequences of α-1 : 4-links did not occur. The type 1 absorption together with the type 3 absorption at 765 cm.$^{-1}$ provided a strong indication that the principal link was α-1 : 6 in type. Again there was no absorption maximum at 793 $\pm$ 3 cm.$^{-1}$ corresponding with 1 : 3-links. Thus the spectrum of polymaltose was similar to, but not quite identical with, that of polyglucose.

Polymers were readily obtained from galactose, from lactose, and from a mixture of galatose with glucose, as shown in the Table. Their structures are being examined.

We are greatly indebted to Dr. M. Heidelberger who tested the serological reactivity of some of these polysaccharides (cf. Heidelberger and Aisenberg, *Proc. Nat. Acad. Sci. U.S.A.*, 1953, **39**, 453; Heidelberger, Aisenberg, and Hassid, *J. exp. Med.*, 1954, **99**, 343). Polymaltose reacted more heavily with pneumococcus Type XII antiserum than polyglucose but both left some antibody reactive with glycogen. There were no precipitates with the Type II antisera used. Polygalactose showed a small but definite precipitate in Type IV antiserum only after long standing and centrifugation; possibly the quantity of polygalactose used was too large in this experiment.

Experimental

Paper Chromatography.—All chromatograms were run on Whatman No. 1 or No. 54 paper in butanol–pyridine–water (6 : 4 : 3 by vol.) (Myrbäck and Willstaedt, *Arkiv Kemi*, 1953, **6**, 417) and sprayed with aniline hydrogen phthalate (Partridge, *Nature*, 1949, **164**, 443).

Polyglucose.—Finely ground glucose monohydrate (9·14% of H_2O) (100 g.) was placed in the rotary mixer into which a delivery tube passed through a glass–glass socket lubricated with Silicone grease. Dry hydrogen chloride was passed through while the mixer rotated for 30 min. The gas was rapidly absorbed and the powder became sticky, adhered to form pellets, and finally became a plastic mass. Rotation was then stopped and the apparatus closed for 5 days. The viscous mass was then dissolved in ice-cold N-sodium hydroxide solution, neutralised, dialysed, and decolorised with charcoal. On evaporation under reduced pressure to 92 ml. a small quantity of insoluble material separated and was rejected. Addition of ethanol (92 ml.) precipitated a syrup which was hardened in ethanol, washed with ether, and dried *in vacuo* over phosphoric oxide, yielding polyglucose (P 2) (see Table). The supernatant solution yielded on evaporation more polyglucose (12·0 g.) consisting of short-chain material, bringing the total yield of soluble non-dialysable polymer to 45%.

Polyglucose (P 3) (see Table) was prepared in the same way, the total yield of polymer being 46%.

Polyglucose (P) (see Table) was obtained by combining the products of five similar preparations. By careful fractional precipitation it was obtained free from saccharides mobile on a paper chromatogram.

Polygalactose.—Galactose (0·75% of H_2O) (50 g.) in a thin layer covering a dish 16 cm. in diameter was placed in a desiccator containing concentrated hydrochloric acid. The crystals slowly deliquesced to a pale brown syrup. After 7 days at room temperature the syrup was worked up as above, yielding a brown polygalactose (10·18 g.). Evaporation of the supernatant solution yielded a further 3·6 g., bringing the total yield to 31%.

The first fraction (10·18 g.) was reprecipitated from ethanol–water, yielding a fraction (5·1 g.) containing all the brown colour and a further fraction (2·8 g., dry basis) (see Table) free from coloured impurity.

Polymaltose.—Maltose monohydrate (6·21% of H_2O) (50 g.) was treated as described for galactose and the polymer was isolated in the same way, yielding polymaltose (16·0 g., dry basis) (see Table), and from the supernatant solution a further 3·0 g. (total yield, *ca.* 47%).

Polylactose.—Lactose (0·29% of H_2O) (50 g.) yielded, under the conditions described for galactose, polylactose (9·9 g., dry basis) free from coloured impurity (see Table). A further 1·6 g. from supernatant solution brought the total yield of polymer to *ca.* 27%.

Polymer from Glucose–Galactose Mixture.—Finely ground galactose (20 g.) was moistened with water (2 ml.) and after storage in a closed container for 20 hr. to attain, as far as possible, a uniform distribution of moisture, the mixture was ground with glucose monohydrate (20 g.). The mixture was placed in the rotary mixer, and dry hydrogen chloride was passed through it for 30 min. The product was isolated as described for polyglucose. At 50% v/v ethanol a fraction (7·3 g., dry basis) was precipitated. From the supernatant solution a further 4·2 g. was isolated (total yield of non-dialysable polymer, *ca.* 36%).

Polymerisation of Glucose for 19 Hours and Examination of Oligosaccharides.—Glucose monohydrate (100 g.) was exposed to anhydrous hydrogen chloride as described above. After 19 hr. the mixture was dissolved in excess of cold N-sodium hydroxide, and the solution neutralised, decolorised with charcoal, and concentrated to 37 ml. After removal of the insoluble matter (0·424 g.), polyglucose was precipitated as a syrup by the addition of ethanol (74 ml.). The syrup was ground in alcohol, washed twice with alcohol and twice with ether, and dried *in vacuo* (yield 24·51 g.; $[\alpha]_D$ +88°; reducing value 5·4).

Polyglucose (5 g.), dissolved in water (10 ml.), was passed down a column, 33 cm. long and 2 cm. in diameter, of a 1 : 1 mixture of washed B.D.H. activated charcoal and Hyflo Supercel (Whistler and Durso, *loc. cit.*). The column was washed with water and then aqueous ethanol (8%), and eluted fractions were collected and their optical rotations measured.

From the eluate a freeze-dried white powder (0·267 g.) was obtained which on paper chromatography gave a spot with an R_F value identical with that of glucose (0·43) and a second spot with an R_F value of 0·28 close to that of *iso*maltose and different from that of the laminaribiose in a laminarin hydrolysate. Electrophoresis of the same material in 0·2M-sodium borate (Foster, *loc. cit.*) showed four spots with M_G values 1·03, 0·75, 0·70, and 0·32, identical with those from a mixture of glucose, gentiobiose, *iso*maltose, and maltose.

Partial Hydrolysis of Polyglucose (P) and Chromatography.—A solution of polyglucose (0·6 g.) in water (6 ml.) was centrifuged to remove the small amount of insoluble matter. The solution (1 ml.), mixed with 2N-sulphuric acid (1 ml.), was heated in a sealed ampoule at 100° for 62 min. The cooled hydrolysate was neutralised with excess of barium carbonate, and the solid filtered off and washed. The combined washings and filtrate were concentrated to 1 ml.; the electrical conductivity was $1{\cdot}05 \times 10^{-3}$ μmhos. The hydrolysate showed on paper chromatography at 35° for 18 hr. spots with R_G 1·00, 0·57, and 0·26, and the controls (dextran hydrolysate) spots with R_G values 1·00, 0·57, 0·30, and 0·15.

Effect of Conditions of Hydrolysis on Glucose.—Glucose (0·1 g.), dissolved in 2 ml. of N-sulphuric acid, was heated in a sealed ampoule at 100° for 75 min. The solution was de-salted with barium carbonate and concentrated to 0·5 ml. Paper chromatography showed only a very faint trace of disaccharide and no higher saccharides. Polyglucose hydrolysate chromatographed on the same paper showed a readily detectable quantity of disaccharide as well as of higher saccharides.

Partial Hydrolysis of Polyglucose and Separation of Oligosaccharides.—Polyglucose (P) (10·00 g.) was fractionated further by reprecipitation from its aqueous solution (30 ml.) with absolute alcohol (43·5 ml.). The precipitated syrup was poured into excess of alcohol (500 ml.),

and the white solid washed with ether and dried *in vacuo* (P_2O_5) (yield 6·38 g.; $[\alpha]_D$ +115·5°; reducing value 34·8). No saccharides mobile on a paper chromatogram could be detected.

A solution of this purified polyglucose (5·81 g.) in water (58 ml.) was heated with stirring on a boiling-water bath for 30 min. Sulphuric acid (58 ml.; 2N) was added dropwise during 5 min. The mixture was heated for a further 65 min. and then cooled rapidly. $[\alpha]_D$ was then +69·4° (*c*, 5). The hydrolysate was immediately passed down a column, 33 cm. long and 4·5 cm. in diameter, of a 1 : 1 mixture of B.D.H. activated charcoal and Hyflo Supercel. After adsorption of the hydrolysate the column was washed with water followed by water–ethanol mixtures of increasing ethanol content. After most of the sulphuric acid had been washed off the column (before the saccharides), excess of barium carbonate was added to the eluate fractions [which were slightly acid (pH 4—5·5)]. Measurement of optical rotation of the eluate showed three main peaks, and the corresponding fractions were combined, filtered, and distilled to dryness under reduced pressure. The residues were extracted successively with hot methanol and hot water (products I and II), or hot ethanol and hot water (product III). The alcoholic and the aqueous extracts were combined and from the extract of product I a white solid crystallised (810 mg.). Products II (388 mg.) and III (898 mg.) were isolated as freeze-dried powders. Product I when chromatographed on paper gave a single spot corresponding to glucose and was further characterised by conversion into β-glucose penta-acetate, m. p. and mixed m. p. 130—131°. Product II was shown by paper chromatography and borate electrophoresis (Foster, *J.*, 1953, 982) to be *iso*maltose. A portion (0·151 g.) was heated with fused anhydrous sodium acetate (0·800 g.) and acetic anhydride (1·50 ml.) at 100—110° for 1 hr. (cf. Barker, Bourne, Bruce, Neely, and Stacey, *J.*, 1954, 2395) to give a product which on repeated recrystallisation from absolute ethanol gave a crystalline acetate, m. p. 147·6—148·0° (*iso*maltose octa-acetate prepared from *iso*maltose obtained from a dextran hydrolysate had m. p. 146·2—147°). Product III when subjected to paper chromatography and to ionophoresis in borate buffer gave two spots corresponding to the *iso*maltotriose and *iso*maltotetraose in a dextran hydrolysate.

Partial Hydrolysis of Polymaltose.—Polymaltose (0·10 g.) was heated in N-sulphuric acid (2 ml.) at 100° for 75 min. in a sealed ampoule. The cooled hydrolysate was neutralised with barium carbonate, filtered, and concentrated to 0·5 ml. A spot of this solution was chromatographed on Whatman No. 54 paper and compared with dextran hydrolysate, polyglucose hydrolysate, and maltose on the same paper. Polymaltose hydrolysate showed spots with R_G values 1·00, 0·54, 0·27, and 0·16; polyglucose hydrolysate 1·00, 0·55, 0·26, and 0·15; and dextran hydrolysate 1·00, 0·52, 0·25, and 0·14; maltose showed R_G 0·73.

Periodate Oxidation of Polyglucose and Polymaltose.—Polyglucose (0·0995 g.) which had been freeze-dried and dried to const. wt. *in vacuo* (P_2O_5 at 100°) was oxidised in 100 ml. of 0·0355M-sodium metaperiodate. The formic acid produced (Jeanes and Wilham, *J. Amer. Chem. Soc.*, 1950, 72, 2655) and the sodium metaperiodate consumed (Fleury and Large, *J. Pharm. Chim.*, 1933, 17, 107, 196) were determined.

Polymaltose (0·0660 g.) was freeze dried and dried to const. wt. in the same way.

Polyglucose: The number of mols. of formic acid produced per anhydroglucose unit was at: 22·7 hr. 0·65; 46·0 hr. 0·71; 71·5 hr. 0·73. And the mols. of sodium metaperiodate consumed were at: 22·8 hr. 1·63; 46·2 hr. 1·59; 71·0 hr. 1·62.

Polymaltose: Corresponding figures were: for formic acid at: 22·4 hr. 0·63; 45·8 hr. 0·70; 71·3 hr. 0·72 mol.; for sodium metaperiodate consumed at: 22·5 hr. 1·57; 45·9 hr. 1·55; 70·8 hr. 1·57 mols.

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The Preparation and Hydrolysis of Some Esters of 2 : 4 : 6-Triphenylbenzoic Acid. Part I. Preparation of the Esters.

By J. Graham and J. R. Quayle.

[Reprint Order No. 6325.]

1 : 3 : 5-Triphenylbenzene was converted into the monobromo-derivative, which was isolated in two forms, one metastable. Oxidative degradation confirmed the structure previously suggested for the monobromide. 2 : 4 : 6-Triphenylbenzoic acid was prepared from the monobromide, and esterified either by the silver salt method or by interaction with diazo-alkanes.

1 : 3 : 5-Triphenylbenzene was most conveniently prepared by condensation of acetophenone with the agency of hydrogen chloride at 60° (Engler and Berthold, *Ber.*, 1874, **7**, 1125). Condensation by means of a mixture of potassium pyrosulphate and concentrated sulphuric acid resulted mainly in the production of tar and a very low yield of 1 : 3 : 5-triphenylbenzene, contrary to the experience of Kohler and Blanchard (*J. Amer. Chem. Soc.*, 1935, **57**, 367).

Two identical methods for the preparation of a monobromo-derivative of 1 : 3 : 5-triphenylbenzene are reported in the literature, by direct bromination in carbon disulphide at room temperature. In one case the melting point of the product was reported as 108° (Engler and Berthold, *loc. cit.*), and in the second as 129° (Kohler and Blanchard, *loc. cit.*). The first sample prepared by the present authors had a melting point of 105—107°, which changed after a few days to 129·5°. All subsequent preparations carried out at the University College of North Wales yielded a product melting initially at 129·5°. The preparation was repeated at University College, London, and on the first occasion yielded a product which melted at 108°, resolidified, and melted again at 129°. On storage the substance changed its initial melting point to 129°, and again all subsequent preparations melted at this temperature. Recrystallisation of the higher-melting form under various conditions also failed to yield the metastable form.

X-Ray powder photographs of the two forms of bromotriphenylbenzene were taken. The samples were mounted in a Lindemann glass capillary, and rotated slowly while being cooled by a stream of liquid air. For ease of comparison both photographs were taken on the same plate by the movable-sector technique. The patterns obtained from the two forms were not identical, indicating a difference of crystalline form or molecular structure.

Two other examples of fugitive melting points in derivatives of *s*-triphenylbenzene are known; 2-cinnamoyl-1 : 3 : 5-triphenylbenzene (Kohler and Blanchard, *loc. cit.*) and *n*-propyl triphenylbenzoate (see below). The persistent glass-like nature of the analytically pure *iso*butyl triphenylbenzoate may also be connected with this behaviour.

It is interesting to speculate whether the compounds in question are monotropic substances, such as benzophenone, or whether the dimorphism results from some restricted rotation of the substituent phenyl groups.

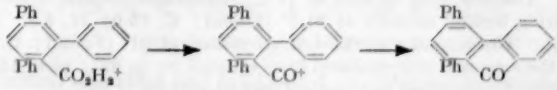
Previously it has been assumed that when triphenylbenzene is brominated, the bromine atom enters the central nucleus. Such arguments as have been adduced for this view are based on steric considerations, *e.g.*, that when the bromine atom is replaced by an acetyl group the product behaves like a methyl ketone with substituents in both *ortho*-positions. For a study of the effect of *ortho*-substituents on the hydrolysis of esters of the required triphenylbenzoic acid a more direct proof of the position of the bromine atom in the molecule was felt to be desirable. The position taken up by the bromine atom is limited to the central nucleus, or to one of the six available *ortho*-positions in the three substituent phenyl groups, by the observation that attempts to prepare triphenylbenzoyl chloride from the derived triphenylbenzoic acid resulted only in the formation of 1 : 3-diphenylfluorenone (Kohler and Blanchard, *loc. cit.*). Oxidation might, therefore, be expected to yield either a mixture of bromotrimesic and benzoic acid, or of trimesic, benzoic, and *o*-bromobenzoic acid, the last two in the proportion of 2 : 1 (cf. the oxidation of nitrotriphenylbenzene; Vorlander Fischer, and Willie, *Ber.*, 1929, **62**, 2836). Numerous

oxidations were carried out, but in every case the main product of the reaction was benzoic acid. The only other product, obtained in very small amount, was an acid with an equivalent weight corresponding roughly to that of a bromodiphenylbenzoic acid. Both *o*-bromobenzoic acid and bromotrimesic acid (a crude sample was prepared by oxidation of bromomesitylene) are known to be stable under the reaction conditions employed, and it was observed that *o*-bromobenzoic acid can be separated from relatively large quantities of admixed benzoic acid by chromatography of aqueous solutions of their sodium salts on a column of alumina, first washed with dilute nitric acid, then washed neutral with water. Careful analysis, using this method, of the benzoic acid product from the oxidations failed to reveal any admixed *o*-bromobenzoic acid.

The failure to detect *o*-bromobenzoic acid suggests that the bromine atom is located in the central nucleus, also that in such a system the central nucleus is very much more susceptible to oxidising agents than the substituent phenyl groups.

1 : 3 : 5-Triphenylbenzoic acid was prepared from bromotriphenylbenzene by the Grignard reaction with xylene as solvent and diethylaniline as catalyst (Kohler and Blanchard, *loc. cit.*), and with less initial difficulty by using dibutyl ether as solvent (Marvel *et al.*, *J. Amer. Chem. Soc.*, 1928, **50**, 2810).

Methyl (Kohler and Blanchard, *loc. cit.*), ethyl, *n*-propyl (dimorphic), *iso*propyl, *iso*butyl, and *tert.*-butyl triphenylbenzoate were prepared, either by the silver salt method, or by interaction of the acid with the appropriate diazo-alkane in ethereal solution. Other methods of esterification were unsatisfactory. In particular, reaction of the acid with the appropriate alcohol in concentrated sulphuric acid solution, a method normally successful with "sterically hindered" acids (Meyer, *Monatsh.*, 1904, **25**, 1201), resulted only in the formation of 1 : 3-diphenylfluorenone, presumably owing to the formation, and immediate cyclisation in this medium, of an acylium ion from the acid. Formation of this intensely yellow fluorenone derivative would, therefore, provide evidence for the incursion of Day and Ingold's mechanism *A*'1 (*Trans. Faraday Soc.*, 1941, **37**, 686), subsequently $A_{Ac}1$, in acid-catalysed hydrolysis of these esters.



Kohler and Blanchard (*loc. cit.*) have reported adversely on the application of the silver salt method of esterification to triphenylbenzoic acid. However, the method succeeds if the silver salt is prepared by double decomposition of the sodium salt with silver nitrate. Direct interaction of the acid with silver nitrate gives a precipitate which actually contains much co-precipitated silver nitrate, and reaction of this with an alkyl halide naturally results in a poor yield of ester.

Experimental

Oxidation of 1-Bromo-2 : 4 : 6-triphenylbenzene.—1-Bromo-2 : 4 : 6-triphenylbenzene (10 g.) in glacial acetic acid (50 ml.) was heated to *ca.* 95° on a boiling-water bath, and a solution of chromium trioxide (50 g.) in glacial acetic acid (80 ml.) and water (20 ml.) gradually added. The mixture was then poured into a solution of sodium carbonate (400 g.) in water (500 ml.), and the precipitated chromium hydroxide filtered off and washed with hot sodium carbonate solution. On cooling, the combined alkaline filtrates deposited fine crystals. These were filtered off and dissolved in hot water, and the solution was acidified. The resultant precipitate (0·06 g.) was dissolved in aqueous sodium hydroxide, re-precipitated with acid, and finally crystallised from glacial acetic acid, then having m. p. 305—309° (Found : equiv., 372. Calc. for $C_{19}H_{13}O_2Br$: equiv., 353).

The alkaline filtrate was then acidified with nitric acid and exhaustively extracted with ether. Evaporation of the ethereal extract yielded pure benzoic acid (6 g.). Chromatography of the sodium salt showed that no *o*-bromobenzoic acid was present.

2 : 4 : 6-Triphenylbenzoic Acid.—A conventional Grignard apparatus was modified by the addition of a tap sealed on to the base of the flask, and the provision of an exterior asbestos mantle carrying an electric heater. The apparatus was first flooded with nitrogen, and then

ethyl bromide (7 ml.) in diethyl ether (100 ml.) was added to magnesium turnings (5 g.) in the flask. When the reaction became vigorous, the apparatus was drained through the attached tap, solid bromotriphenylbenzene (26 g.) and di-*n*-butyl ether (30 ml.) containing a trace of iodine were immediately added, the flow of nitrogen being maintained, and the flask was then heated until reaction commenced. More di-*n*-butyl ether (250 ml.) was run in during 30 min.; then, slowly, so that reaction was maintained, bromotriphenylbenzene (20 g.) in xylene (100 ml.) was added. After this the mixture was boiled for 3 hr., then cooled, and a slow current of dry carbon dioxide passed in, through a wide delivery tube, for 3 hr. A white solid separated. Sulphuric acid (25 ml.) in water (75 ml.) was added and the organic solvents were removed in steam. The semi-solid residue was separated by filtration and extracted with boiling benzene (100 ml.), and the filtered benzene solution shaken when cold with an excess of aqueous sodium hydroxide. A brown layer of sodium triphenylbenzoate formed between the two layers. This was separated and boiled with dilute sulphuric acid. The resultant white triphenylbenzoic acid (30 g.) was crystallised from glacial acetic acid; it had m. p. 251° (Found : C, 85·3; H, 5·1. Calc. for $C_{25}H_{18}O_2$: C, 85·7; H, 5·1%).

Ethyl 2 : 4 : 6-*Triphenylbenzoate*.—An ethereal solution of diazoethane was prepared from ethylamine (20 g.) (Adamson and Kenner, *J.*, 1935, 286; 1937, 1554), and cooled to 0°. Solid triphenylbenzoic acid was added gradually with stirring, until the yellow colour of the solution was discharged. Excess of acid was removed by extraction with aqueous sodium hydroxide, and the solution then dried and concentrated. The resultant *ethyl* 2 : 4 : 6-*triphenylbenzoate* (25 g.), recrystallised from ethanol, had m. p. 95° (Found : C, 85·9; H, 6·1. $C_{27}H_{22}O_2$ requires C, 85·7; H, 5·8%).

n-*Propyl* 2 : 4 : 6-*Triphenylbenzoate*.—*n*-Propylamine (25 g.) was converted into diazopropane by the method of Adamson and Kenner (*loc. cit.*). Concentration of the mixture yielded a colourless oil, crystallisable from ethanol. Two crops of crystals were obtained, having m. p. 72·5° and 92° respectively. These were combined, a 70% solution in benzene chromatographed through alumina, and the column developed with a 2% solution of ethanol in benzene. Under ultraviolet light two narrow zones were visible at the top of the column, which on elution with ethanol yielded only traces of material. The colourless non-fluorescent lower section of the column was also eluted with ethanol. Evaporation yielded three successive crops of crystals. The first crop melted at 72·5°, resolidified, melted again at 91·5°, and on cooling and reheating melted initially at 91·5° (Found : C, 85·6; H, 6·3. $C_{28}H_{24}O_2$ requires C, 85·7; H, 6·1%). The second and third crops melted at 91° (Found : C, 86·2; H, 6·5%). The main bulk of the *ester* was recrystallised from ethanol (m. p. 92°; yield 15 g.).

A sample prepared by the silver salt method melted initially at 92°.

iso*Butyl* 2 : 4 : 6-*Triphenylbenzoate*.—Diazo*iso*butane was prepared from *iso*butylamine (25 g.) and treated with triphenylbenzoic acid as above. Evaporation yielded an oily *ester* (4 g.) which was poured in benzene (30 c.c.) on alumina (27 × 2·5 cm.) and eluted with benzene. The appearance of the ester in the eluate was detected by measuring the refractive index of successive 5-c.c. samples. The solution containing the purified ester on evaporation yielded a colourless gum with no definite m. p.; it did not crystallise (Found : C, 85·1; H, 6·6. $C_{29}H_{26}O_2$ requires C, 85·7; H, 6·4%).

Silver 2 : 4 : 6-*Triphenylbenzoate*.—Triphenylbenzoic acid (19 g.) was dissolved in hot ethanol (350 c.c.) and exactly neutralised with aqueous 1·04N-sodium hydroxide. On addition of silver nitrate (9·3 g.) in water (30 c.c.) a creamy-white precipitate of the silver salt was obtained. This was filtered off, washed with 1 : 1 ethanol–water, and dried *in vacuo* (yield 21·3 g.).

Methyl 2 : 4 : 6-*Triphenylbenzoate*.—Silver triphenylbenzoate (15 g.), methyl iodide (24 c.c.), and di-*n*-butyl ether (80 c.c.) were refluxed together for 2 hr., then cooled, and filtered from silver iodide, and the solvent was removed under reduced pressure. The residual yellow oil, crystallised from methanol–acetic acid, had m. p. 89·5°.

The ester was also prepared by use of ethereal diazomethane (Kohler and Blanchard, *loc. cit.*); it then had m. p. 91° (Found : C, 85·2; H, 5·2. Calc. for $C_{26}H_{20}O_2$: C, 85·7; H, 5·5%).

iso*Propyl* 2 : 4 : 6-*Triphenylbenzoate*.—Silver triphenylbenzoate (3·87 g.), *iso*propyl iodide (4 c.c.), and benzene (10 c.c.) were heated at 95° for 12 hr. The mixture was then filtered, extracted with aqueous sodium hydroxide, dried, and evaporated. The residual reddish oil was dissolved in ether and extracted with aqueous sodium thiosulphate to remove iodine. The dried solution on evaporation yielded the *ester* which, crystallised from glacial acetic acid, had m. p. 82° (0·4 g.) (Found : C, 85·0; H, 6·0. $C_{28}H_{24}O_2$ requires C, 85·7; H, 6·1%).

tert.-*Butyl* 2 : 4 : 6-*Triphenylbenzoate*.—Silver triphenylbenzoate (54 g.), *tert.*-butyl bromide (48·5 g.), and benzene (150 c.c.) were shaken together in a glass-stoppered bottle for 24 hr.

Filtration, extraction with aqueous sodium hydroxide, and evaporation yielded the *ester* which, crystallised from ethanol, had m. p. 101·5° (34 g.) (Found : C, 85·9; H, 6·5. $C_{25}H_{20}O_2$ requires C, 85·7; H, 6·4%).

Attempted Esterification in Sulphuric Acid.—Triphenylbenzoic acid (1 g.) was shaken with 100% sulphuric acid (20 c.c.) for 10 min. and the dark solution then poured into cold methanol (200 c.c.). The mixture was concentrated, diluted with water, and extracted with ether, and the combined extracts were evaporated to dryness. The residual yellow solid was poured in benzene (15 c.c.) on a column of alumina, the column developed with benzene containing 5% of ether, and the prominent yellow zone cut out and eluted with ethanol. Evaporation yielded 1 : 3-diphenylfluorenone, m. p. and mixed m. p. 182—183°. Nothing was obtained by elution of the remaining part of the column.

Separation of o- *and* p-*Bromobenzoic and Benzoic Acid.*—A 3% aqueous solution of equal parts of the sodium salts of benzoic, *o*-bromobenzoic, and *p*-bromobenzoic acid was poured on a 60-cm. column of alumina, which had been washed with N-nitric acid and then washed neutral with water. The column was developed with water (50 c.c.) and cut arbitrarily into 3-cm. sections which were eluted with water. The order of adsorption from the top of the column was *o*-bromobenzoate, benzoate, and *p*-bromobenzoate.

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Preparation and Hydrolysis of Some Esters of 2 : 4 : 6-Triphenylbenzoic Acid. Part II. The Mechanisms of Hydrolysis.*

By C. A. Bunton, A. E. Comyns, J. Graham, and J. R. Quayle.

[Reprint Order No. 6326.]

The reactions of methyl and *tert.*-butyl 2 : 4 : 6-triphenylbenzoates have been followed kinetically in aqueous methanol and in aqueous dioxan under initially neutral conditions and in the presence of acids and bases. By the use of ^{18}O as tracer the positions of bond fission have been determined.

With the methyl ester bimolecular attack on both the acyl- and the alkyl-carbon atom is observed in the presence of alkali, but the *tert.*-butyl ester gives alkyl–oxygen bond fission, with formation of a carbonium ion, under all conditions investigated.

Qualitative observations have been made on the rates of hydrolysis of other esters of this acid.

The reactions of 2 : 4 : 6-triphenylbenzoic acid in the presence of mineral acid have been examined chemically and isotopically.

This work provides examples of all the present known mechanisms of carboxyl esterification and hydrolysis. It illustrates the powerful steric hindrance of the *o*-phenyl groups to nucleophilic attack on the acyl-carbon atom and shows that this effect does not operate on the alkyl-carbon atom.

The availability of a number of esters of 2 : 4 : 6-triphenylbenzoic acid (Graham and Quayle, Part I *) has made possible a mechanistic study of the reactions of these compounds in aqueous methanol and in aqueous dioxan. The choice of solvents was dictated by solubility requirements.

Preliminary kinetic experiments on the reactions of primary and secondary alkyl 2 : 4 : 6-triphenylbenzoates in aqueous 95% methanol showed these compounds to be unusually resistant to nucleophilic attack under both acid and alkaline conditions, whereas

* Part I, preceding paper.

the *tert.*-butyl ester was solvolysed in neutral or alkaline solutions at a rate independent of the alkali concentration, but dependent on the acid concentration.

The resistance of the esters of the primary and secondary alcohols to reaction in alkaline and dilute acidic media, conditions which normally lead to bimolecular attack on the acyl-carbon atom (mechanisms $B_{AC}2$ and $A_{AC}2$; Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686), is largely due to the powerful steric hindrance of the two *o*-phenyl groups. The *tert.*-butyl ester shows no such resistance to solvolysis; in fact its solvolysis rates are qualitatively similar to those of other *tert.*-butyl esters. It appears that this ester undergoes solvolysis by mechanisms independent of bimolecular attack on the acyl-carbon atom, and isotopic experiments prove alkyl–oxygen bond fission.

In concentrated sulphuric acid 2 : 4 : 6-triphenylbenzoic acid and its esters give 1 : 3-diphenylfluorenone (Part I). However, in dilute hydrochloric acid in aqueous dioxan a very slow oxygen exchange between the acid and water is observed, presumably occurring by the mechanism $A_{AC}2$, which is subject to the steric hindrance of the *o*-phenyl groups.

It appears therefore that the esters of 2 : 4 : 6-triphenylbenzoic acid provide a suitable system for a study of some of the less readily realisable mechanisms of ester hydrolysis, and a detailed study has been made of the kinetic form and the position of bond fission of the methyl and the *tert.*-butyl ester in aqueous methanol and aqueous dioxan, and qualitative observations have been made on the reactions of the esters of various primary and secondary alcohols in aqueous methanol.

Experimental

Preparation of Materials.—Methyl, ethyl, *n*-propyl, *iso*propyl, *iso*butyl, and *tert.*-butyl 2 : 4 : 6-triphenylbenzoate were prepared and purified by the methods described in Part I.

Solvents.—Methanol was purified and dried by Lund and Bjerrum's method (*Ber.*, 1931, **64**, 210). The aqueous methanol used as solvent was prepared by adding 5 vols. of water to 95 vols. of methanol.

Dioxan was purified as described by Vogel ("Practical Organic Chemistry," Longmans Green, 1948, p. 175). The aqueous dioxan was prepared by adding 3 vols. of water to 7 vols. of dioxan.

Kinetic Measurements.—Kinetic runs were followed in sealed tubes. Thick-walled Pyrex test tubes were used for kinetic runs under acidic and initially neutral conditions, and for alkaline runs in aqueous methanol. This procedure was not satisfactory for the alkaline runs, as prolonged heating at high temperatures caused considerable attack of the alkali on the glass: control tests were carried out and a correction was made for this attack. This, of necessity, reduced the accuracy of the rate measurements in alkaline methanol, and metal containers were investigated.

The most satisfactory metal was found to be silver, and containers with suitable side-arms for the addition and removal of the solutions were manufactured by Messrs. Johnson and Matthey to a design of Dr. Budd. The side-arms of the filled tubes were sealed in an oxy-coal gas flame and were opened by cutting off the tips. Thus the difficulties were removed and silver tubes were used in all the alkaline hydrolyses in aqueous dioxan.

Kinetic runs were followed by acid–alkali titration in absence of carbon dioxide, either by an indicator method (bromothymol-blue), with bromothymol-blue as a colour standard for sodium triphenylbenzoate, or by a potentiometric method with a glass electrode. The latter method, being free from subjective errors, was preferred, and was used in the later work.

Examples of kinetic runs on the methyl and *tert.*-butyl esters are tabulated. $(a - x)$ and $(b - x)$ are the respective concentrations of ester and OH^- at various times.

Alkaline hydrolysis of methyl 2 : 4 : 6-triphenylbenzoate in aqueous dioxan at 120°.

[Ester] = 0·0462M, [OH^-] = 0·0404M. Samples of 5·11 c.c. were taken, added to 5 c.c. of 0·07N-H_2SO_4, and titrated with 0·0125N-NaOH.

Time (hr.) ...	—	16·7	40·5	64·5	88·7	113·5	151	175	176	99·2	251
Titre (c.c.) ...	3·6, 3·7	7·4	11·3	11·8	13·4	14·7	16·5	16·8	17·2	18·0	18·4
$\log \frac{a}{b}\left(\frac{b-x}{a-x}\right)$	—	0·016	0·046	0·051	0·074	0·101	0·161	0·179	0·203	0·283	0·32
$10^5 k_2$	—	8·7	10·4	7·2	7·6	8·2	9·7	9·3	10·5	13·0	11·6

Mean value of $10^5 k_2$ = 9·0 mole^{-1} l. sec.$^{-1}$.
(Value from slope of log $[(b - x)/(a - x)]$ against t, $10^5 k_2$ = 11·3 mole^{-1} l. sec.$^{-1}$.)

Neutral hydrolysis of tert.*-butyl 2 : 4 : 6-triphenylbenzoate in aqueous dioxan at* 135°.

[Ester] = 0·047M. Samples of 5·15 c.c. were taken and titrated with 0·01N-NaOH.

Time (hr.) ...	0	1·6	2·5	4·0	5·5	7·0	8·0	23·2	25·7	29·7	47·2	55·2
Titre (c.c.) ...	0·3	2·2	3·4	4·6	6·1	7·1	7·8	15·7	16·5	17·5	22·7	23·2
$\log [a/(a-x)]$	—	0·036	0·060	0·085	0·119	0·144	0·161	0·440	0·481	0·539	1·129	1·270
10^5k_1	—	1·44	1·53	1·35	1·38	1·32	1·28	1·21	1·20	1·16	1·53	1·45

Mean value of 10^5k_1 = 1·35 sec.$^{-1}$.
[From the slope of log $(a-x)$ against t, 10^5k_1 = 1·39 sec.$^{-1}$]

Qualitative estimates of the reactivities of the ethyl, *n*-propyl, *iso*propyl, and *iso*butyl esters in aqueous 95% methanol were made by measuring the amount of acid produced in 72 hr. at 118·5°. Allowance was made for the attack of the alkali on the glass. The alkali was *ca.* 0·05M, and the ester was *ca.* 0·02M. The % reactions were: Me 61; Et 17; β-methylated, Pr^n 6·5, Bu^i 6; α-methylated, Pr^i 3, Bu^t 72, 72·5.

In view of the possibility of the reaction, $R{\cdot}CO_2R + OMe^- \rightleftharpoons R{\cdot}CO_2Me + OR^-$, occurring in 95% methanol more precise determinations of the reactivities of the various esters in this sytem were not undertaken.

Under initially neutral and acid conditions (N/20-benzenesulphonic acid), in aqueous methanol, no solvolysis was detected for the methyl, ethyl, *n*-propyl, *iso*propyl, and *iso*butyl esters after 48 hr. at 118·5°. Prolonged heating resulted in explosion of the glass tubes, presumably owing to formation of dimethyl ether from the aqueous 95% methanol.

No hydrolysis of the methyl ester was observed in aqueous 70% dioxan in initially neutral and acidic conditions during 11 days at 120°.

A summary of the kinetic results is tabulated.

Tracer Studies.—In all tracer studies the water was isotopically enriched, and the ester, or acid, was initially of normal abundance. The low solubilities of the esters in the aqueous solvents, and their high molecular weights, precluded the isolation of the alcohol product in quantities sufficient for an isotope analysis, and such an isolation would have been valueless in reactions in aqueous methanol. Therefore the isotopic abundance of oxygen in the 2 : 4 : 6-triphenylbenzoic acid product was determined.

TABLE 1. *Solvolyses in aqueous methanol.*

(i) *Neutral and alkaline reactions.* Temp., 118·5°. Solvent, aqueous 95% methanol.

(*a*) Me ester + OMe^- : 10^5k_2 = 5·5, 6·7, 5·7 mole^{-1} l. sec.$^{-1}$.
(*b*) Bu^t ester + 95% MeOH : 10^6k_1 = 5·25 sec.$^{-1}$.*
" + 0·0333M-H_2O in MeOH : 10^6k_1 = 2·91 sec.$^{-1}$.*
" + 0·0555M-H_2O in MeOH : 10^6k_1 = 2·94 sec.$^{-1}$.*
" + OR^-(R=H or Me) : 10^6k_1 = 4·9 sec.$^{-1}$.

* Extrapolated to zero time.

(ii) *Acid-catalysed reactions of* tert.*-butyl ester.*

Solvent, 95% methanol.			Solvent, methanol with small quantities of water.			
Temp.	$[H^+]$	10^4k_A (mole^{-1} l. sec.$^{-1}$)	Temp.	$[H_2O]$	$[H^+]$	10^3k_A (mole^{-1} l. sec.$^{-1}$)
80·0°	0·0540	23·8	80·0°	0·0344	0·0516	11·8
"	0·0406	24·3	65·2	0·0333	0·0687	2·37
70·1	0·0585	7·20	"	0·0555	0·0509	2·28
"	0·0535	7·25				

$k_1 = k_A[H^+]$.

TABLE 2. *Hydrolyses in aqueous 70% dioxan.*

$[OH^-]$	Temp.	10^7k_1 (sec.$^{-1}$)	$[OH^-]$	Temp.	10^5k_2 (mole^{-1} l. sec.$^{-1}$)
Bu^t *ester*			Me *ester*		
—	101·2°	3·76	0·055	120·0°	11·3
—	120	24·4			
—	135	139			
0·050	120	22·0			

After reaction (which was usually not carried to completion because of the low reaction rates), most of the organic solvent was removed under reduced pressure, and the triphenylbenzoic acid and unchanged ester were separated. The acid was converted into its silver or calcium salt, and the salt, after intensive drying in a high vacuum, was decarboxylated by heat. The silver salt was used for the decarboxylation of the acid obtained from hydrolysis in aqueous dioxan, and the calcium salt for most of the products of reactions in aqueous methanol.

The oxygen isotopic abundance of the carbon dioxide was determined by mass-spectrometry. The ratio of abundances, R, of masses 44 and 46 (corresponding to $^{12}C^{16}O^{18}O$ and $^{12}C^{16}O^{18}O$), was determined. Then if α is the atom % abundance of ^{18}O in the carbon dioxide, then $\alpha = 100/(2R + 1)$ atoms %.

The isotopic abundances were always compared with a standard sample of gaseous carbon dioxide, prepared by the decarboxylation of normal 2 : 4 : 6-triphenylbenzoic acid. The values of isotopic abundances quoted are the excess abundance of a sample above that of a normal sample.

The isotopic abundance of the water used was in general determined by equilibration with gaseous carbon dioxide, followed by mass spectrometry of the carbon dioxide. The isotopic abundance, α, of the water is given by $\alpha = 100/(KR + 1)$, where $K = 2{\cdot}076$ at 25°.

The isotopic abundances of one sample of enriched water (that used in the blank tests and solvolyses of the *tert.*-butyl esters in aqueous methanol) was estimated from a density determination carried out by Dr. D. R. Llewellyn.

The isotopic analyses on samples obtained from reactions in aqueous methanol were (with two exceptions, experiments W5 and X18) carried out by the Mass Spectrometer Group of the Atomic Energy Research Establishment, Didcot. Other isotope analyses were carried out on a 180° mass spectrometer of conventional design.

Under all conditions control experiments were carried out to ensure that the presence or absence of tracer was not due to extraneous exchange, or to isotopic discrimination, in the isolation or decarboxylation of the triphenylbenzoate. The standard normal sample of acid had an excess isotopic abundance (determined by decarboxylation) of 0·002 atoms % greater than that of normal cylinder carbon dioxide.

The results of the tracer experiments are in Tables 3—5.

TABLE 3. *Reactions in* 95% *methanol.*

Experiment		^{18}O abundance (atoms % excess) :		
No.	Description	in H_2O	in acid isolated	O_2 derived from H_2O (%)
B1	Untreated acid	—	0·00	—
B2	Control for B3; 130°	0·80	0·001	—
B3	Neutral; Bu^t ester; 3 days; 130°	0·80	0·001	—
B4	0·08M-Acid; Bu^t ester; 1½ days; reflux	0·80	0·00	—
B5	Control for B4; reflux	0·80	0·00	—
B6	Control for W5 & X18; 120°	0·80	0·00	—
W5	0·064M-NaOH; Me ester; 13 days; 120° *	0·532	0·033	6·2
X18	As W5; 9 days *	1·156	0·075	6·5

* In Ag tube.

Isolation of Dimethyl Ether.—An attempt was made to isolate dimethyl ether after reaction of the methyl ester (1·04 g.) in aqueous 95% methanol with M/30-alkali at 120° for 40 days. As this reaction was carried out under kinetic conditions the quantity of ether formed was expected to be small. The ether was fractionated through a low-hold-up column with a gas take-off.

TABLE 4. *Blank tests in aqueous* 70% *dioxan at* 120°.

Experiment			^{18}O abundance (atoms % excess):	O_2 derived from
No.	Description	Days	in H_2O	in acid or ester	solvent (%)
W20	Neutral Na salt	11	0·300	0·001	—
W21	Alkaline Na salt	10	0·300	0·002	—
W2	Acid alone	100	0·532	0·002	—
W3	Acid + 0·7M-HCl	100	0·532	0·142	26·5
X4	,,	100	1·156	0·315	27
X10	Me ester + 0·07N-NaOH	13	,,	0·133, 0·162 *	11·5, 14

* Ester isolated and pyrolysed (both expts.).

The distillate contained some material of low volatility, which was removed by static distillation in a high vacuum. The purified ether had M 48 and comprised 80% of the original distillate. The purification by static distillation and the measurement of molecular weight by vapour density were carried out by Dr. Joan Banus.

The yield of ether was 45%. A parallel experiment on a solution of dimethyl ether gave an overall recovery of *ca.* 60%. Although these results are only qualitative they show that some dimethyl ether is formed by bimolecular attack of the methoxide ion on the alkyl-carbon atom of methyl 2 : 4 : 6-triphenylbenzoate.

TABLE 5. *Hydrolyses in aqueous dioxan.* (Excess abundance of ^{18}O in H_2O, 1·156%.)

Expt. no.	Concn. (%) of dioxan	Conditions	[Ester] (M)	^{18}O Abundance in acid (atoms % excess)	O_a derived from solvent (%)
But ester					
X1	70	0·02M-H_2SO_4 (18 hr.)	0·030	0·00	—
X2	,,	Neutral (14 days)	0·037	0·00	—
X11	,,	Alkali (14 days)	0·037	0·003	—
Me ester					
X8	70	0·07M-NaOH (13 days)	0·043	0·716	62
X5	,,	,, ,,	0·060	0·684	59
X6	,,	0·049N- ,,	0·060	0·653	56·5
X7	,,	0·042N- ,,	0·060	0·638	55
X12	75	0·025N-NaOH (14 days)	0·027	0·653	56·5
X13	73	,, ,,	,,	0·653	56·5
X14	71	,, ,,	,,	0·644	55·5
X15	70	,, ,,	,,	0·648	56
X16	69	,, ,,	,,	0·638	55

DISCUSSION

Position of Bond Fission.—In principle the position of bond fission in ester hydrolysis can be determined unambiguously by the use of ^{18}O as a tracer. This classic method has frequently been used (Polanyi and Szabo, *Trans. Faraday Soc.*, 1934, **30**, 508; Datta, Day, and Ingold, *J.*, 1939, 838), with isolation and isotopic assay of the alcohol product. In the present work it has been necessary to follow the tracer in the acid product; alkyl–oxygen fission gives an acid containing no isotopic tracer.

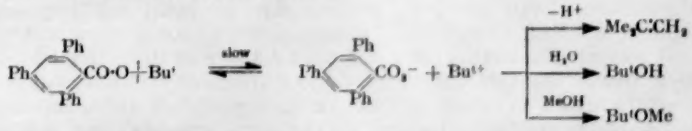
Bimolecular acyl–oxygen bond fission may give an exchange between the oxygen atoms of the water and the carbonyl-oxygen atoms of the ester (Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626).

In the hydrolysis of methyl 2 : 4 : 6-triphenylbenzoate in alkaline aqueous dioxan the ester was recovered from a partial hydrolysis, and was found to be isotopically enriched (Expt. X10), showing that oxygen exchange of the methyl ester occurred during hydrolysis. In view of Bender's similar observations on the benzoates (*loc. cit.*), we did not feel justified in raising this to a quantitative level. It is because of this exchange reaction of the ester molecule that the isotopic abundances of the methyl 2 : 4 : 6-triphenylbenzoate exceeds half that of the water (Experiments X5—8, 12—16 incl.).

The results for the methyl ester in aqueous dioxan show that the predominant fission was of the acyl–oxygen bond. They do not exclude the existence of a small amount of alkyl–oxygen bond fission in the alkaline hydrolysis, since the effect of this mechanism in giving no tracer in the acid could be masked by the oxygen exchange of the ester.

An increase in alkali concentration gives a small increase in the isotopic abundance in the isolated acid, whereas an increase in the water content of the solvent has the opposite effect. This dependence on the water content of the solvent may be due to a small amount of alkyl–oxygen bond fission (by mechanisms $B_{AL}2$ or $B_{AL}1$), which would probably be favoured by an increase in the water content of the solvent.

Isotopically normal acid is obtained in the solvolyses of *tert.*-butyl 2 : 4 : 6-triphenylbenzoate in both aqueous dioxan and aqueous methanol, proving alkyl–oxygen bond fission. Preliminary experiments (carried out by Mr. B. Stephenson) showed that considerable amounts of *iso*butene were formed in the alkaline solvolyses, and as the kinetic measurements show no rate acceleration by alkali we may depict the solvolysis of this ester in initially neutral and alkaline solutions thus:



The reactions of the methyl 2 : 4 : 6-triphenylbenzoate in aqueous methanol in the presence of methoxide ion are complicated by the co-existence of hydrolysis and methanolysis.

Four simultaneous reactions are possible :

Acyl–oxygen bond fission :

(*a*) $R{\cdot}CO{-}OMe + {}^{18}OH^- \longrightarrow R{\cdot}CO{\cdot}{}^{18}O^- + Me{\cdot}OH$

(*b*) $R{\cdot}CO{-}OMe + MeO^- \longrightarrow R{\cdot}CO{\cdot}OMe + MeO^-$

Alkyl–oxygen bond fission :

(*c*) $R{\cdot}CO{\cdot}O{-}Me + {}^{18}OH^- \longrightarrow R{\cdot}CO{\cdot}O^- + Me{}^{18}OH$

(*d*) $R{\cdot}CO{\cdot}O{-}Me + MeO^- \longrightarrow R{\cdot}CO{\cdot}O^- + MeOMe$

Only reactions (*a*), (*c*), and (*d*) will give identifiable products, as reaction (*b*) in this special case merely regenerates the methyl ester. Only reaction (*a*) introduces tracer into the acid. Experiments W5 and X18 show that in aqueous methanol fission of the alkyl–oxygen bond predominates, although it does not disclose whether the reagent is the hydroxide or the methoxide ion; and, as there is no precise knowledge of the position of the equilibrium under our conditions, for the reaction, $MeOH + OH^- \rightleftharpoons MeO^- + H_2O$ (cf. Caldin and Long, *J.*, **1954**, 3737), the relative concentrations of these ions are unknown. Isolation of dimethyl ether from the reaction of the methyl ester in alkaline aqueous methanol at 120° shows that reaction (*d*), attack of the methoxide ion on the alkyl-carbon atom, does occur. It may be that in aqueous 95% methanol all the isotopically normal acid is produced by methanolysis, and that hydrolysis gives attack on the acyl-carbon atom only, for the isolation experiment was not sensitive enough to test this. These experiments give no information on the attack of the methoxide ion on the acyl-carbon atom (reaction *b*), as this could be observed only by isotopic labelling of the methyl group on carbon or hydrogen.

The formation of dimethyl ether by the attack of methoxide ion in methyl alcohol, on the alkyl-carbon atom of methyl benzoate (Bunnett, Robinson, and Pennington, *J. Amer. Chem. Soc.*, **1950**, **72**, 2328), shows that bimolecular attack on the methyl group of a methyl ester can occur under conditions similar to those of our experiments in aqueous 95% methanol.

Kinetic Form and Mechanism of Reaction.—The 2 : 4 : 6-triphenylbenzoates of primary and secondary alcohols studied in this work decompose only in the presence of alkali. We can therefore exclude, for them, all mechanisms which involve ionisation of the neutral ester molecule or reaction of its protonated species.

In aqueous dioxan the values of the second-order rate coefficients for the alkaline hydrolysis of the methyl ester, together with the tracer experiments, show that the predominant mechanism is $B_{AC}2$. In this solvent the steric hindrance by the two *o*-phenyl groups is sufficient to make the acyl-carbon atom relatively insensitive to nucleophilic attack, but it is insufficient to make this attack slower than ionisation of a methyl carbonium ion from the neutral molecule or slower than attack of the hydroxide ion on the alkyl-carbon atom.

The kinetic form of the hydrolysis of *tert.*-butyl 2 : 4 : 6-triphenylbenzoate in neutral and alkaline aqueous dioxan, and the demonstration of alkyl–oxygen bond fission show that the rate-determining step is the ionisation of the neutral ester molecule (mechanism $B_{AL}1$), a reaction strictly analogous to the well-defined S_N1 reactions of alkyl halides.

In aqueous 95% methanol reaction rate decreases with increase in the length of the alkyl group for esters of various primary and secondary alcohols : but these measurements were qualitative and their interpretation is complicated by trans-esterification. The last reaction will generate the methyl ester, the most reactive of the group considered, and will therefore reduce any rate differences. The decrease of rate observed is consistent with nucleophilic attack on either the alkyl- or the acyl-carbon atom, and as the tracer results for the alkaline reaction of the methyl ester in this solvent show that both modes of attack occur, attempts to interpret these results quantitatively would not be justified.

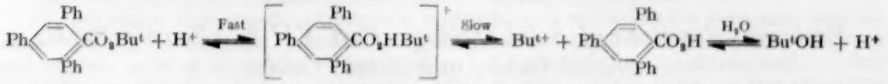
In aqueous methanol the solvolysis of *tert.*-butyl 2 : 4 : 6-triphenylbenzoate is not accelerated by the addition of alkali; in fact the rate in initially neutral solution is slightly

greater than the rate in the presence of alkali. A small anticatalytic effect of the hydroxide ion is typical of many S_N1 reactions (Benfey, Hughes, and Ingold, *J.*, 1952, 2494), but this interpretation is complicated by the observation of slight anticatalysis in the neutral reaction. This rate increase in the course of the run (which is not observed with the *tert.*-butyl ester in aqueous dioxan) is presumably due to catalysis by the triphenylbenzoic acid, or by the protons derived from it.

As would be expected, this solvolysis, in which the formation of a carbonium ion from the neutral ester molecule is the rate-determining step, is facilitated by an increase in the water content of the solvent. The effect is not large, suggesting that the methanol molecules are comparable to the water molecules in their ability to solvate the partially formed carbonium ion. This is in marked contrast to the effect of a change of water content in the aqueous dioxan used as solvent in the hydrolysis of triphenylmethyl acetate by mechanism $B_{AL}1$ (Bunton and Konasiewicz, *J.*, 1955, 1354). In this system, where the solvent effect is very marked, the dioxan molecules presumably make very little contribution to the solvation of the partially formed carbonium ion.

In sharp contrast to the primary and secondary alkyl triphenylbenzoates, the *tert.*-butyl ester shows a very marked acid catalysis of solvolysis in aqueous methanol.

The isotopic results prove alkyl–oxygen bond fission by mechanism $A_{AL}1$:



Because of the ease of hydration of *iso*butene under acid conditions no attempt was made to identify an elimination product in this reaction. It would be expected, however, that the carbonium ion would be partitioned between substitution and elimination, as in solvolysis in neutral or alkaline solution.

The effect of a change in the water content of the aqueous methanol solvent is in the opposite direction to that observed for the neutral reaction. The solvent effect in an acid-catalysed ester solvolysis (*e.g.*, $A_{AL}1$) is two-fold, an effect on the pre-equilibrium proton transfer, and one on the breakdown of the protonated ester molecule.

The tendency of hydrochloric acid to donate a proton to a neutral base has been shown to decrease on the addition of small amounts of water to ethanol (Braude and Stern, *J.*, 1948, 1976; and activity measurements); this is probably true also for the addition of small amounts of water to methanol. Therefore the addition of water to methanol will lower the equilibrium concentration of the protonated ester, and hence decrease the reaction rate. In other systems in which the $A_{AL}1$ mechanism is observed (triphenylmethyl and *tert.*-butyl acetates in aqueous dioxan), the rate of decomposition of the protonated ester increases with increase in the water content of the solvent. It seems therefore that in aqueous methanol the water is little more effective than methanol in solvating the partially formed carbonium ion, but is more effective in holding the protons, and that the latter effect in decreasing the rate outweighs the former effect in increasing it.

For the solvolyses of *tert.*-butyl 2 : 4 : 6-triphenylbenzoate the parameters A and E of the Arrhenius equation $k = Ae^{-E/RT}$ are :

In initially neutral aqueous 70% dioxan,

$A = 3{\cdot}2 \times 10^{12}$ sec.$^{-1}$, $E = 32{\cdot}4$ kcal. mole^{-1} (from 3 temp.).

In acidic aqueous 95% methanol,

$A = 3{\cdot}7 \times 10^{15}$ mole^{-1} l. sec.$^{-1}$, $E = 29{\cdot}3$ kcal. mole^{-1} (from 2 temp.).

The activation energy for the ionisation of this tertiary alkyl ester molecule is therefore *ca.* 32 kcal. mole^{-1}, and the value of the activation energy for the acid-catalysed solvolysis is 29·3 kcal. mole^{-1} [cf. the value of *ca.* 30 for the acid-catalysed solvolysis of *tert.*-butyl trimethylbenzoate in aqueous ethanol (Stimson and Watson, *J.*, 1954, 2848), a reaction which presumably involves alkyl–oxygen bond fission]. This suggests that the heat content for the protonation of a tertiary alkyl ester is small compared with the activation energy for the formation of a carbonium ion from it.

These mechanisms and examples of the systems in which they are observed may be summarised as follows:

Acyl–oxygen fission. $B_{AC}2$. Hydrolysis of methyl ester in aqueous dioxan. It also occurs to some extent with this ester in aqueous methanol.

$A_{AC}2$. Observed only in oxygen exchange of the acid in aqueous dioxan.

$A_{AC}1$. Not observed in hydrolysis. Its existence is demonstrated by the formation of 1 : 3-diphenylfluorenone by the action of sulphuric acid on the acid or its esters.

Alkyl–oxygen fission. $B_{AL}1$. The *tert.*-butyl ester in neutral or alkaline solutions.

$B_{AL}2$. Occurs to some extent with the methyl ester in alkaline aqueous methanol. It may not occur with OH^- as the reagent, under these conditions.

$A_{AL}1$. Observed in solvolysis of the *tert.*-butyl ester in acidic aqueous methanol.

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Exchange Reactions of Solid Oxides. Part VII. Chromic Oxide, Nickel Oxide, and Ferric Oxide.*

By E. R. S. Winter.

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The rates of isotopic exchange between gaseous oxygen and the oxide surface, and of the equilibration of molecular oxygen catalysed by the oxide, have been examined by use of the technique described in earlier papers. On all three oxides the exchange and equilibration reactions occur at the same speed; the studies were performed mainly at $P_{O_2} \approx 6$ cm. and the approximate temperature ranges and apparent activation energies, in kcal. mole^{-1}, are: Fe_2O_3, 290—400°, $E = 19 \pm 2$, rate $\propto P_{O_2}^{1\cdot0}$; NiO, 390—590°, $E = 35 \pm 2$; rate independent of P_{O_2}; Cr_2O_3, 270—530°, $E = 32 \pm 2$ below 430° and 1—2 above, both rates independent of P_{O_2}. The rates of adsorption of oxygen on these oxides obey the Elovich equation, with the activation energy for adsorption rising in a roughly linear manner from ~0 at zero coverage to ~35 (NiO, Cr_2O_3) or >12 (Fe_2O_3) at saturation. The rates of adsorption are proportional to P_{O_2} over the whole range, but the saturation coverages, in terms of the total exchangeable surface, are small. It is concluded that the exchange–equilibration reaction is in all cases (but for Cr_2O_3 only below 430°) a measure of the rate of adsorption–desorption of oxygen; above 430° on Cr_2O_3 either the rate of migration of chemisorbed oxygen or that of surface defects in the solid is rate-determining. Limited mobility of chemisorbed oxygen on the surface of NiO at 250—300° has been directly demonstrated.

The semiconductivities of the oxides have been measured over the same temperature range in oxygen at various pressures and *in vacuo*: no direct correlation has been found between semiconductivity and isotopic exchange or oxygen adsorption.

The total surfaces of the oxides determined by oxygen exchange, by B.E.T. isotherm, and, in the case of Fe_2O_3, by adsorption of Fe^{3+} from aqueous solution, are compared: good agreement is obtained between the various methods.

The techniques described in Parts I—VI* have been used to examine in detail the interaction of gaseous oxygen and the oxides Cr_2O_3, NiO, and Fe_2O_3; since these oxides adsorb appreciable amounts of oxygen at temperatures and pressures approaching those of interest

* Parts I—VI, *J.*, 1950, 1170, 1175; 1954, 1509, 1517, 1522; 1955, 2726.

here, it has been possible to study the kinetics of adsorption and to relate them to the exchange and equilibration reactions. The dependence of the semiconductivity of the oxides upon oxygen pressure and upon the degree of outgassing has been studied. The oxide most thoroughly studied was chromic oxide and this work is described in the greatest detail, since the behaviour of this oxide was generally typical; work on the other oxides is presented in an abbreviated form, except for some observations upon the determination of the surface area of Fe_2O_3 by use of radioactive iron. The symbols, where undefined, are those used in earlier papers.

Experimental

(a) *Materials.*—Cr_2O_3 was prepared by controlled ignition of "AnalaR" CrO_3 in a stream of dry air (Bevan, Shelton, and Anderson, *J.*, 1948, 1729); two preparations were used, made from different batches of CrO_3. NiO was prepared by ignition of the carbonate in air at 850° for 6 hr.: B.D.H. carbonate of low cobalt and iron content was used. Fe_2O_3 was prepared by reaction of ferric chloride solution with aqueous ammonia, followed by copious decantation and washing, and ignition in air at 500° (cf. Gregg and Hill, *J.*, 1953, 3945; Hill, Ph.D. Thesis, London, 1950).

Enriched, non-equilibrated, and normal oxygen were as previously described (*J.*, 1954, 1522).

(b) *Adsorption Experiments.*—Adsorption isotherms were studied in the apparatus used for earlier work (*J.*, 1954, 1509), pressures being measured on two McLeod gauges and a mercury manometer; rates of adsorption were studied in a constant-pressure apparatus similar to that of Taylor and Strother (*J. Amer. Chem. Soc.*, 1934, **56**, 586); at low pressures this apparatus was actuated by a Pirani gauge instead of a mercury manometer. Certain rates of adsorption were measured under constant-volume conditions. Nitrogen adsorption isotherms for B.E.T. area calculations were determined at liquid-nitrogen temperatures in an apparatus like Gregg and Sing's (*J. Phys. Colloid Chem.*, 1951, **55**, 592).

(c) *Exchange and Equilibration.*—The kinetics were studied as in earlier work (*locc. cit.*).

(d) *Electrical Conductivity.*—The stainless steel conductivity "cell" was of the same design as that of Jacobs (*J. Sci. Instr.*, 1953, **30**, 204): the pellet was made by compression in a stainless-steel press and was outgassed for some days (as noted under each oxide) at about 510° before the commencement of observations; 2—12 v D.C. was applied to opposite faces of the pellet, and the current measured on a sensitive galvanometer (sensitivity 5×10^3 mm. μA^{-1} at 1 m.). It was noted at each oxygen pressure whether the pellet obeyed Ohm's law and whether conductivity at each point was independent of the direction of current flow. Readings were taken at random, with both rising and falling temperature, to confirm absence of drift.

(e) *Radioactive-iron Experiments.*—These refer to only one oxide and are discussed in detail under Fe_2O_3.

(f) *General.*—Temperatures above room temperature were continuously controlled to $\pm\frac{1}{2}°$ by an electronic controller actuated by a platinum-resistance coil wound directly on to the silica tube of the furnace, under the heater windings.

Results.—(*a*) Cr_2O_3. The exchange reaction rate for Sample B was independent of outgassing temperature over the range 395—630° and of P_{O_2} over the range 2·5—8·6 cm. (Table 1). The plot of $\log_{10}(k_0 n_s)$ against $10^6/T$ for Samples A and B is shown in Fig. 1; the

Table 1. Cr_2O_3 (B): *Variation of exchange rate with pressure.*

Temp. Outgassing	Temp. Reaction	$\log_{10}(kn_s)$	P_{O_2}	Temp. Outgassing	Temp. Reaction	$\log_{10}(kn_s)$	P_{O_2}
630°	394°	18·710	2·5	630°	394°	18·701	8·6
,,	,,	18·722	4·4	510	,,	18·708	6·0
,,	,,	18·720	5·9	395	395	18·690	6·0

two preparations are seen to be very similar, despite the fact that they were made from different batches of CrO_3 and that the work on Sample A was done some years ago at Imperial College with different equipment. We shall consider mainly the results obtained from Sample B, since most of the adsorption and conductivity work was done on this, and for this preparation Fig. 1 gives an apparent activation energy for exchange and equilibration of 32 ± 2 kcal. mole^{-1} below 430°, and of 1—2 kcal. mole^{-1} for exchange above this temperature. Change of n_s with temperature is shown in Table 2.

TABLE 2. Cr_2O_3: *Influence of temperature on* n_s.

Temp. Outgassing	Temp. Reaction	$\log_{10} n_s$	Temp. Outgassing	Temp. Reaction	$\log_{10} n_s$	Temp. Outgassing	Temp. Reaction	$\log_{10} n_s$
Sample A.						Sample B.		
387°	386°	20·297	455°	441°	20·310	630°	326°	19·898
455	323	20·288	527	527	20·342	,,	358	19·895
,,	345	20·283	567	345	20·283	,,	394	19·904
,,	365	20·301	600	367	20·107	,,	447	20·004
,,	391	20·238	,,	374	20·199	,,	485	20·135
,,	410	20·299				,,	522	19·959

A study of the equilibration reaction on Sample B showed that this occurred at the same rate as the exchange reaction, as is seen from Fig. 1, where several points from the equilibration runs are plotted and fall closely on the line drawn through the exchange rates for $E = 32 \pm 2$ kcal. mole^{-1}. Equilibration runs at temperatures above 430°, the inflexion temperature in the Arrhenius plot for the exchange reaction, were not possible as the rate was too great for accurate measurement.

A typical adsorption–desorption isotherm on Sample A at 395° is shown in Fig. 2, and in

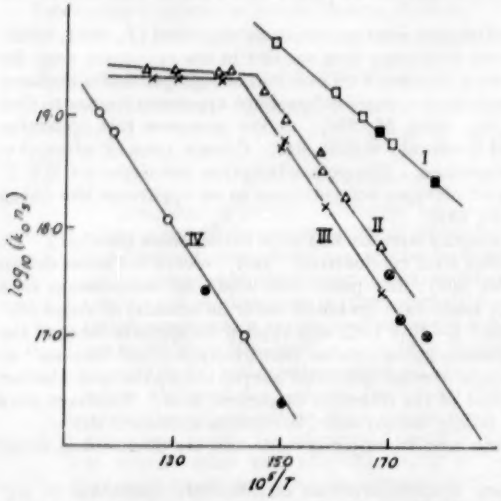


FIG. 1. *Exchange and equilibration experiments.*

□ ■ Exchange and equilibration on Fe_2O_3, outgassed at 450°; $P_{O_2} = 5{\cdot}7$ cm.
△ Exchange on Cr_2O_3 (A), outgassed at various temperatures between 385° and 520°; $P_{O_2} = 6{\cdot}5$ cm.
× ⊗ Exchange and equilibration on Cr_2O_3 (B), outgassed at 630°; $P_{O_2} = 6$ cm.
○ ● Exchange and equilibration on NiO, outgassed at 605°; $P_{O_2} = 6$ cm.

Fig. 3 are shown some rates of adsorption and of exchange, at corresponding temperatures and pressures. As in the exchange experiments, the oxide was outgassed at 520° overnight, isolated, cooled to the required temperature, and then put into contact with the required amount of oxygen; the fall of pressure with time in the constant volume was then recorded, and from the results the quantity adsorbed, expressed as a percentage of the equilibrium value, was calculated. On this basis the rate of adsorption is much greater than the rate of exchange at all temperatures but during desorption appreciable hysteresis occurs. In order to provide more precise information the rates of adsorption on Sample B were determined at constant pressure, mainly at $P_{O_2} = 5{\cdot}9$ cm., and at temperatures from 135° to 240°, which gave rates suitable for measurement. It was found that the uptake, q, followed the law

$$dq/dt = a \exp(-bq) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(cf. Elovich and Zhabrova, *J. Phys. Chem. U.S.S.R.*, 1939, **13**, 1761, 1775; Taylor and Thon, *J. Amer. Chem. Soc.*, 1952, **74**, 4169; Porter and Tompkins, *Proc. Roy. Soc.*, 1953, **217**, *A*, 529).

Integration of eqn. (1) yields (cf. Porter and Tompkins *loc. cit.*):

$$q = \frac{1}{b}\left\{\ln\left(t + \frac{\exp(bq_0)}{ab}\right) + \ln ab\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where q_0 = amount instantaneously adsorbed when $t = 0$.

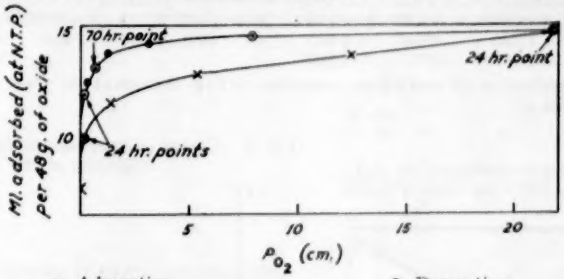
In all our runs [exp (bq_0)]/ab was zero within experimental error, so that $q_0 \approx 0$ (which was confirmed by runs at 10^{-3} mm. of O_2); and straight lines were obtained by plotting q against $\log_{10} t$; from the slopes and intercepts, a and b were evaluated for each temperature and pressure.

From eqn. (1) we have

$$\ln r_s = \ln a - bq \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

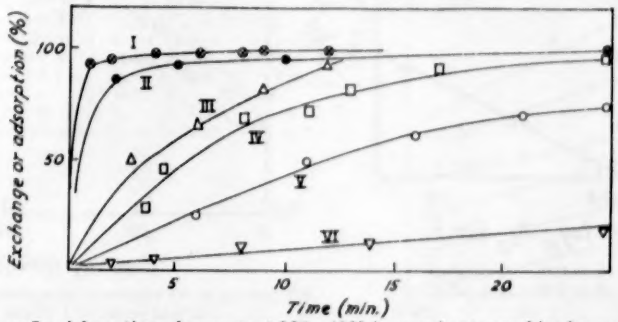
where $r_s = dq/dt$; under our conditions experiments in which ^{18}O was adsorbed up to $\theta \approx 0{\cdot}4$, followed by normal oxygen, established that the rate of desorption was negligible, at least

FIG. 2. *Adsorption–desorption of oxygen on* Cr_2O_3 (*A*) *at* 395°: *oxide outgassed at* 520°.



× Adsorption. ● Desorption.
Circled points refer to readings 24—70 hr. after changing P_{O_2}; remainder to readings taken after 3—4 hr.

FIG. 3. *Adsorption and exchange on* Cr_2O_3 (*A*) *outgassed at* 520°.



Curve I: Adsorption of oxygen at 365—492° (approximate combined curve).
Curve II: Adsorption of oxygen at 325°.
Curves III—VI: Exchange at 493°, 391°, 365°, and 323°, respectively.

up to $\theta \approx 0{\cdot}8$—$0{\cdot}9$ (where $\theta = q/q_\infty$); thus values of r_s from eqn. (3) should be reasonably correct. By using eqn. (3) values of $\log_{10} r_s$ were found at $P_{O_2} = 6$ cm., at different temperatures for $\theta = 0$, 0·22, 0·67, and 0·89; these were plotted against $1/T$ for constant θ, and the apparent activation energy for adsorption, E_a, found at each value of θ; q_∞ did not vary by more than 8% over the temperature range. The results are summarised in Table 3; reasonably straight lines were obtained in the $\log_{10} r_s$–$1/T$ plots, except that the values for $\theta = 0$ (*i.e.*,

TABLE 3. *Adsorption of oxygen on* Cr_2O_3 (B).

		$\log_{10}(r_s)$ *			
Temp. (°K)	$10^5/T$	$\theta = 0$	$\theta = 0{\cdot}22$	$\theta = 0{\cdot}67$	$\theta = 0{\cdot}89$
514	194·5	3·210	2·606	1·407	0·809
465	215	3·043	2·134	0·315	−0·594
433	231	2·876	1·732	−0·530	−1·674
408	245	3·204	1·683	−1·394	−2·933
E_a, kcal. mole^{-1}		~0	9·0	25·3	33·5

* Arbitrary units; to convert to atoms min.$^{-1}$ g.$^{-1}$ add 21·670.

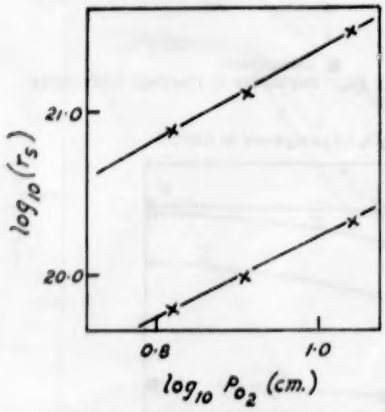
effectively $\log_{10} a$) show some scatter; this is not unexpected in view of the extrapolations involved. A plot of E_a against θ shows that E_a varies linearly from ~0 at $\theta = 0$ to ~35 kcal. mole^{-1} at $\theta \approx 1$. The pressure dependence of r_s was studied at 160° by doing runs at $P_{O_2} = 3{\cdot}5$, 5·9, and 12·3 cm.; the results are summarised in Fig. 4 for $\theta = 0{\cdot}67$ and 0·89; it is evident that r_s is directly proportional to P_{O_2} at these coverages; here also there was some scatter of values at $\theta = 0$: the figures for 3·5 cm. are the mean of the three runs given in Table 4.

TABLE 4. *Adsorption of oxygen on* Cr_2O_3 (B).

		$\log_{10}(r_s)$						$\log_{10}(r_s)$			
Run	q_∞ *	$\theta = 0$	$\theta = 0{\cdot}22$	$\theta = 0{\cdot}67$	$\theta = 0{\cdot}89$	Run	q_∞ *	$\theta = 0$	$\theta = 0{\cdot}22$	$\theta = 0{\cdot}67$	$\theta = 0{\cdot}89$
1	51·5	2·417	1·340	−0·860	−1·937	3	60·0	2·543	1·453	−0·778	−1·868
2	60·7	2·293	1·306	−0·715	−1·702						

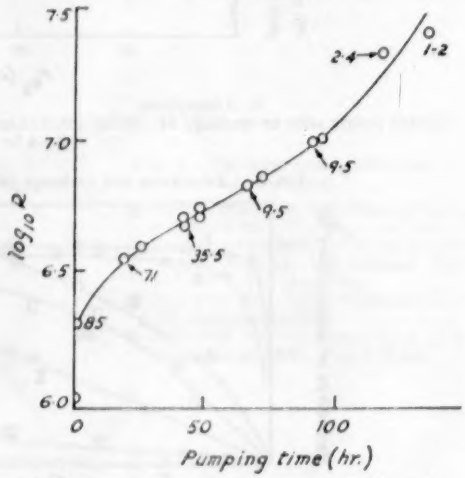
* Ml. of O_2 measured at 17° and 3·5 cm., adsorbed on 10 g. of oxide at 160°; *i.e.*, q_∞ (Runs 2 and 3) $\approx 1{\cdot}4 \times 10^{19}$ atoms g.$^{-1}$.

FIG. 4. *Rate of oxygen adsorption on* Cr_2O_3 *(B), outgassed at 520°: variation of* r_s *with* P_{O_2} *at 160°.*



Upper line: $\theta = 0{\cdot}67$; $r_s \propto (P_{O_2})^{1{\cdot}18}$.
Lower line: $\theta = 0{\cdot}89$; $r_s \propto (P_{O_2})$.

FIG. 5. *Change of semiconductivity of* Cr_2O_3 *on long outgassing at 532°.*



Figures on curve represent pressures (10^{-4} mm.). Initial pressure 1·70 cm.

In order to confirm that $E_a \approx 0$ at $q \approx 0$, 0·1 g. of the oxide was outgassed at 520° and the rates of adsorption of small quantities of oxygen at low pressures were determined, under constant volume conditions, the Pirani gauge being used to follow pressure changes. At 85° and at 103° and mean pressures of 2×10^{-2} mm. the initial rates of adsorption were $2{\cdot}4 \times 10^{20}$ and $2{\cdot}7 \times 10^{20}$ atoms g.$^{-1}$ min.$^{-1}$, which correspond to rates of roughly $7{\cdot}5 \times 10^{23}$ at $P_{O_2} \approx 6$ cm., assuming $r_s \propto P_{O_2}$. Clearly, at these temperatures $E_a \approx 0$ at $\theta \approx 0$; also the initial rate of $7{\cdot}5 \times 10^{23}$ atoms g.$^{-1}$ min.$^{-1}$ is within a power of 10 of that found at higher temperatures and pressures by long extrapolation (Table 3), which is reasonable agreement.

For most of the adsorption work the same 20-g. sample of oxide was employed; the oxide was outgassed at 520° for 18—42 hr. between each run. Preliminary experiments were carried out on a 10-g. sample at 160° and 3·5 cm. pressure to ensure that the reproducibility of the oxide properties was satisfactory between one run and the next. The results are given in Table 4. Although the quantity of oxygen adsorbed at saturation (24 hr.), q_∞, increased appreciably between the first and subsequent runs, all three gave substantially the same values for log a and for log r_s at corresponding coverages: this was confirmed by repeated runs on the 20-g. sample at the completion of the work reported in Table 3. Additional confirmation was provided by running two exchange experiments on portions of oxide which had been used for the adsorption work; satisfactory agreement was obtained (within 7%) of ($k_0 n_s$) with values

found using fresh lots of oxide. The saturation coverage at 406° and 6·0 cm. was about $1·3 \times 10^{19}$ atoms of oxygen per g.: at 321° and 6·0 cm. the coverage was $1·25 \times 10^{19}$ atoms per g.

The B.E.T. surface areas were found in the usual way and call for no comment; an area of 16·2 Å^2 was assumed for the nitrogen molecule; the values found were 30·0 m.^{2} g.$^{-1}$ for Sample A and 14·2 m.^{2} g.$^{-1}$ for Sample B, both specimens being outgassed overnight at 520° before measurement. The n_s values for these two samples were roughly $1·8 \times 10^{20}$ and 8×10^{19} atoms g.$^{-1}$ (Table 2).

The semiconductivity experiments are summarised in Figs. 5 and 6, Fig. 5 showing the decrease of conductivity on prolonged outgassing at a fixed temperature of 532°, and Fig. 6 the change of activation energy, E_σ, for semiconduction with degree of outgassing and with oxygen pressure. When thoroughly outgassed, or in an atmosphere of hydrogen, $E_\sigma = 35 \pm 2$ kcal. mole^{-1}, but at $P_{O_2} > 0·01$ cm., $E_\sigma \approx 11$ kcal. mole^{-1}. Under conditions such that the activation energy is constant at ~11 kcal. mole^{-1}, the semiconductivity increases with P_{O_2} roughly according to $\sigma \propto P_{O_2}^{1/12}$. In all this work the pellets appeared to obey Ohm's, law and the resistance was independent of the direction of current flow: the work in hydrogen was carried out last.

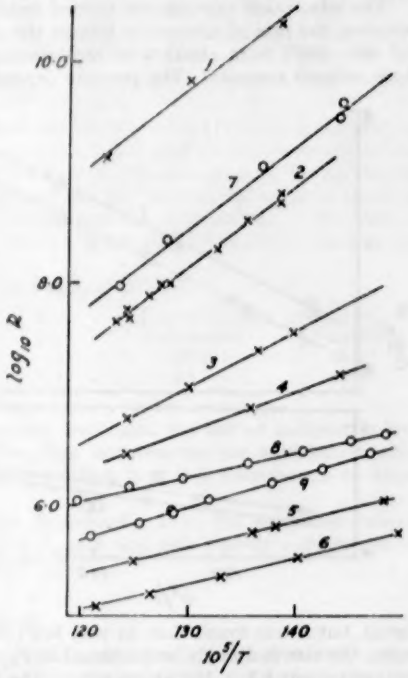


FIG. 6. *Semiconductivity of* Cr_2O_3*—variation with temperature and* P_{O_2}.

× Pellet No. 1, pumped first for 5 days at 532°.
○ Pellet No. 2, pumped first for 2 days at 532°.

Curve 1, $P_{H_2} = 1·1$ cm., $E_\sigma = 36$ kcal.
Curve 2, $P_{O_2} < 10^{-6}$ mm., $E_\sigma = 35$ kcal.
Curve 3, $P_{O_2} = 4·7 \times 10^{-3}$ mm., $E_\sigma = 24$ kcal.
Curve 4, $P_{O_2} = 10^{-1}$ mm., $E_\sigma = 17$ kcal.
Curve 5, $P_{O_2} = 4·6 \times 10^{-1}$ mm., $E_\sigma = 11$ kcal.
Curve 6, $P_{O_2} = 219$ mm., $E_\sigma = 11$ kcal.
Curve 7, $P_{O_2} = 3·5 \times 10^{-5}$ mm., $E_\sigma = 37$ kcal.
Curve 8, $P_{O_2} = 0·14$ mm., $E_\sigma = 10$ kcal.
Curve 9, $P_{O_2} = 120$ mm., $E_\sigma = 13$ kcal.

The Cr_2O_3 as prepared for this work, *i.e.*, after being heated to ~520° in dry air and cooled in air, contained a detectable proportion of chromium in a higher valency state; this was estimated by allowing 1 g. of the oxide to react with acidified potassium iodide solution, centrifuging off the oxide, and titrating the liberated iodine with N/50-thiosulphate (cf. Weller and Voltz, *J. Amer. Chem. Soc.*, 1954, **76**, 4695): similar estimations were made upon 1-g. samples which had been outgassed in high vacuum (*ca.* 10^{-6} mm.) for long peroids, and it was found, as expected, that the oxidising power falls off continuously, but the decrease, amounting only to some 50% in 194 hours' pumping, is not nearly so pronounced as the fall in conductivity on outgassing shown in Fig. 5. These experiments are not very relevant to the main object of the present paper, but will be reported in detail later in another connection.

For the purpose of this set of experiments, the 1-g. samples were sealed in separate tubes to a common vacuum line and sealed off one by one; for titration, the tubes were broken under the surface of the potassium iodide solution so that the outgassed oxide did not come into

contact with the air until it had reacted. An aqueous extract of the original oxide sample, tested with diphenylcarbazide (cf. Feigl, "Spot Tests—Inorganic Applications," p. 162, Elsevier, 1954), gave a strong reaction for chromate.

(*b*) NiO. Only a limited amount of exchange and equilibration work has been done with this oxide. It has been established that, for samples outgassed at 605° overnight: (*a*) n_s is about 10^{20} atoms g.$^{-1}$, varying slowly with reaction temperature from $1{\cdot}1 \times 10^{20}$ at 570° to $6{\cdot}3 \times 10^{19}$ at 486°; (*b*) equilibration and exchange occur at the same speed; (*c*) the apparent activation energy of the exchange–equilibration reaction is 35 ± 2 kcal. mole^{-1}; (*d*) the latter reaction is independent of P_{O_2} over the range 1·5—10·0 cm. The results are not quoted in detail, but the Arrhenius plot is given in Fig. 1 together with those of the other oxides. Over the temperature range covered there is no sign of the abrupt change of slope in the Arrhenius plot that was found with Cr_2O_3 (and MgO and ZnO; Parts III and IV, *locc. cit.*).

The adsorption experiments yielded results very similar to those obtained with Cr_2O_3; for instance, the rate of adsorption follows the same law [eqns. (1) and (2) above], with E_a rising (at 400—460°) from about 0 at zero coverage to about 38 ± 3 kcal. mole^{-1} at saturation at 6 cm. oxygen pressure. The pressure dependence of the rate of adsorption was not studied in

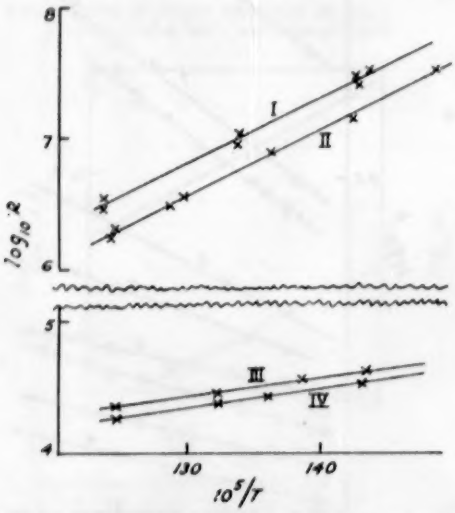


FIG. 7. *Semiconductivity of* NiO*—variation with temperature and* P_{O_2}*: pumped first for 2 days at 520°.*

Curve I, $P_{O_2} = 2 \times 10^{-5}$ mm., $E_\sigma = 22$ kcal.
Curve II, $P_{O_2} = 10^{-4}$ mm., $E_\sigma = 22$ kcal.
Curve III, $P_{O_2} = 3{\cdot}6$ cm., $E_\sigma = 7$ kcal.
Curve IV, $P_{O_2} = 14{\cdot}8$ cm., $E_\sigma = 7$ kcal.

detail, but it was found that, at very low coverages in the pressure range 2×10^{-3} to 2×10^{-2} mm., the rate is directly proportional to P_{O_2}. The saturation oxygen coverage at 407° and 5·7 cm. was about $1{\cdot}3 \times 10^{18}$ atoms g.$^{-1}$. The B.E.T. (N_2) surface was 5·5 m.^{2} g.$^{-1}$.

The semiconductivity phenomena, very similar to those of Cr_2O_3, are summarised in Fig. 7; E_σ varies from 23 ± 2 kcal. mole^{-1} in a high vacuum to 7 ± 1 kcal. mole^{-1} in presence of oxygen. This oxide is not so regular in its behaviour as Cr_2O_3, some lack of reproducibility being experienced; in a few cases the resistance depended on the direction of current flow and in this event the mean resistance has been recorded: the uncertainty was never more than 10%. In the presence of oxygen the pellet acquired a surface layer containing excess of oxygen, becoming grey-black in contrast to the grey-green of the evacuated oxide.

(*c*) Fe_2O_3. The exchange and equilibration reactions (see Fig. 1) occur at the same speed, and $E \approx 19 \pm 2$ kcal. mole^{-1}; n_s is approximately constant at $\sim 6{\cdot}5 \times 10^{20}$ atoms g.$^{-1}$ at 300—400°. In contrast to the other two oxides, the rate of exchange–equilibration is directly proportional to $P_{O_2}^{1\cdot0}$ at 1·7—10·2 cm.

Owing to the relatively small amount of oxygen adsorbed and to the slow rate of attainment of equilibrium it was not possible to measure rates of oxygen adsorption at pressures of several cm. on this oxide. At $P_{O_2} \leqslant 2$ mm. (mainly at 10^{-2}—10^{-3} mm.) the rate of adsorption measured at 85—250° on oxide outgassed at 500° follows the same law as on the other two oxides, with $E_a \approx 0$ at $q \approx 0$, rising to at least 12 kcal. mole^{-1} near "saturation" at $P_{O_2} = 1{\cdot}5$ mm.* and

* The saturation value for q is inaccurate since not only did q increase slowly during 24 hr. at 1·5 mm., but q also showed a slow increase with increasing P_{O_2}.

appears to be proportional to P_{O_2}. "Saturation" at 4 cm. pressure at 277° corresponds to an adsorption of about $5{\cdot}6 \times 10^{17}$ atoms g.$^{-1}$: the B.E.T. (N_2) surface area is 33·5 m.^{2} g.$^{-1}$.

An attempt was made to measure the surface area of the oxide by exchange of iron between the surface and ferric chloride solution containing Fe-55/59. No exchange was detected but it proved possible to perform the desired measurement by following the adsorption of radioactive iron from solution. The radioactive iron, obtained from A.E.R.E., Harwell, was diluted with iron carrier to give a N/10-solution of ferric chloride with a count in a liquid counter of 12,000—15,000 min.$^{-1}$. For several such solutions, adjusted to different pH's with hydrochloric acid or ammonia, the iron content was determined by titration with permanganate by the Zimmermann–Reinhardt method; 15 ml. of these solutions were agitated in stoppered tubes for 24 hr. with 0·1 g. of Fe_2O_3 in a rotary shaker, and the iron content and radioactive count found in 10 ml. of the clear supernatant liquid obtained by centrifugation. The results are shown in Table 5.

TABLE 5. *Stability of* Fe_2O_3 *at various* pH.

pH	1·1	1·15	1·28	1·50	1·94	2·2
Change of Fe^{3+} content (%) in solution in 24 hr.	+392	+14	−1	−8	−18	−24

There was no significant loss of radioactivity from the solution when the oxide was dissolving (*i.e.*, below about pH 1·2) but the loss of Fe^{3+} from solution found analytically above pH 1·2 was parallel to the loss of radioactive iron. 0·1-g. lots of the oxide were shaken at *ca.* 18° for varying times with ferric chloride solution adjusted to a chosen pH 2·2, determined by glass electrode and a commercial pH meter, and the total iron content and the radioactivity of the solution determined: the results, given in Table 6, show that an exact parallelism exists between iron

TABLE 6. *Adsorption on* Fe_2O_3 *at* pH 2·2.

Time (hr.)	Loss of Fe from solution (%): Radioactive	Titration	Time (hr.)	Loss of Fe from solution (%): Radioactive	Titration
½	6·4	0·9	51½	31·0	29·8
1	11·9	11·7	113	36·1	36·9
20½	23·7	26·1			

lost from the solution by adsorption on the powdered oxide and the loss of radioactive iron determined by counting: assuming that the adsorption isotherm reaches equilibrium when ~40% of the iron in solution has been adsorbed, we find that this corresponds to about $5{\cdot}3 \times 10^{20}$ atoms of Fe per g. of oxide.

The semiconductivity measurements were less reproducible than for the other oxides; conductivity is high *in vacuo* (48 hr. at 500°) with $E_\sigma \approx 2$, and falls rapidly with increasing P_{O_2}; E_σ at $P_{O_2} \approx 0{\cdot}5$ mm. upwards ≈ 22 kcal. mole^{-1}.

DISCUSSION

The semiconductivity measurements were undertaken to see whether any relation exists between the activation energies characteristic of this property and those found for the exchange reactions. No such relation was detected but the experiments merit discussion. The work was performed with D.C. voltages; as it is now well known that a correct interpretation of such work in terms of semiconductivity theory is difficult owing to the great influence of high (or low) conductivity surface states on the pellet conductivity, a wide frequency range should be used (cf. Henisch, *Phil. Mag.*, 1951, **42**, 734; Verwey, Reading Conference on Semi-Conductors, 1950, Butterworths, 1952, p. 151; Volger, *Phys. Rev.*, 1950, **79**, 1023). It is therefore noteworthy that our measurements agree in general with recent results of other workers using the same technique; thus, with E_σ in kcal. mole^{-1}: Cr_2O_3, present work **35** and **11**; Bevan, Shelton, and Anderson (*loc. cit.*) **32** and **7—14**; Chaplin, Chapman, and Griffiths (*Proc. Roy. Soc.*, 1954, **224**, *A*, 419) ~**31** and **14**: Fe_2O_3, present work ~**2** and **22**; Bevan, Shelton, and Anderson **8·5** and **25**; Morin (*Phys. Rev.*, 1951, **83**, 1005) — and **25** (A.C. measurement): NiO, present work **23** and **7**; Morin (*ibid.*, 1954, **93**, 1199) **23** and ~**10** (A.C. and D.C.); Hogarth (*Proc. Phys. Soc.*, 1951, **64**, *B*, 691) "green" ~**22**, "black" ~**11**; Parravano (*J. Chem. Phys.*, 1955, **23**, 5) — and **9**. In this list the first figure of each pair refers to measurements in a high vacuum or in hydrogen, and the second to measurements in several cm. of air or oxygen:

they are for roughly the same temperature ranges as ours. Our results are very similar to those of Anderson *et al.*, and the slow drift of conductivity of Cr_2O_3 on prolonged pumping (Fig. 5) is like that recorded by them for ZnO (cf. also Bevan and Anderson, *Discuss. Faraday Soc.*, 1950, **8**, 238); we have found, as expected, the same effect with NiO and Fe_2O_3. All three oxides, when fully reduced (*i.e.*, evacuated thoroughly at ~500°), can adsorb small quantities of oxygen at low pressure without any effect on the conductivity. When the quantity adsorbed became sufficient to change the conductivity it was noted that the addition of a charge of oxygen causes an immediate change in resistance, followed by a slow drift to equilibrium. On all three oxides at around 400° and pressures of 10^{-2}—10^{-3} mm. the equilibrium takes an hour or more to be attained, but is fairly rapidly reached at 500° (cf. Bevan and Anderson, *loc. cit.*). This effect may well be due to a slow redistribution of the adsorbed oxygen over the interior surface of the compressed pellet: in this connection it was noted that the NiO pellet, after a series of measurements in oxygen, had a blackened surface, the interior remaining grey-green, but the blackening did not extend fully under areas covered by the tightly-clamped platinum electrodes. Clearly, true equilibrium was never attained in the presence of oxygen with this material and therefore possibly not in the case of the others: this probably did not affect the limiting values for E_a, which were reproducible from one pellet to another, in several cm. of oxygen and in a vacuum or hydrogen, but may have altered the intermediate figures and the absolute values of resistance recorded, but in the present context these are not important.

Our conductivity results for Cr_2O_3 (Figs. 5 and 6), taken with the results of other workers mentioned above (cf. also Weisz, Prater, and Rittenhouse, *J. Chem. Phys.*, 1953, **21**, 2236), confirm the view that (subject to the uncertainty introduced by the surface states, which uncertainty will not disappear until much higher temperatures where very rapid oxygen exchange between gas and solid may occur) in the presence of oxygen this oxide is a *p*-type conductor, containing a (surface) excess of oxygen as O^-_{ads} or O^{2-}_{ads} and a proportion of its (surface) chromium in a 4- or 6-valent state. In hydrogen or other reducing atmosphere, or if thoroughly outgassed, the oxide probably passes through an intrinsic state to become an *n*-type conductor, possibly containing excess of metal. Similarly Fe_2O_3 is an *n*-type conductor while NiO is of *p*-type: the mechanism of semiconduction in these two oxides is uncertain (Morin, Parravano, *locc. cit.*).

We refer now to the remainder of the experimental work, and assume that the conclusions of the adsorption experiments can be applied over the whole of the temperature range used in the exchange–equilibration work. It appears that on Cr_2O_3 and NiO the exchange–equilibration reaction as measured is the rate of adsorption–desorption of oxygen (the reaction of $E \approx 2$ above ~430° on Cr_2O_3 will be considered later): the same probably applies to Fe_2O_3 but here the adsorption results are not conclusive enough to be sure of this. Thus we can say that on exposure to oxygen the freshly-outgassed oxide adsorbs the gas (forming almost certainly O^-_{ads}, with consequent change in conducting properties) with an activation energy for adsorption, E_a, which rises approximately linearly with coverage from zero to about 35 kcal. mole^{-1} (for Cr_2O_3 and NiO, and probably ~20 kcal. mole^{-1} for Fe_2O_3) at saturation when $P_{O_2} = 6$ cm.; at the same time the activation energy for desorption, E_d, must fall similarly from some value $\leqslant 35$ kcal. mole^{-1} * (say $\leqslant 20$ for Fe_2O_3) until at saturation $E_a = E_d$. The rate of desorption then governs the observed rate of exchange–equilibration.

The fact that $r_a \propto P^{\frac{1}{2}}_{O_2}$ for an adsorption process which is almost certainly dissociative presents no difficulty when it is noted that the coverages, in terms of fractions of the total surface, n_a, are all small around 6 cm., *viz.*, 15% (Cr_2O_3), 1—2% (NiO), 0·1% (Fe_2O_3).

In the case of Cr_2O_3 and NiO, the surface is effectively saturated with oxygen well below 6 cm., so that the exchange–equilibration reaction is pressure-independent; on Fe_2O_3 the latter reaction is directly proportional to P_{O_2} and it is considered that the coverage is still increasing over the range 1·7—10·2 cm., although this could not be directly demonstrated owing to the small amount of oxygen adsorbed on this oxide, and, as noted earlier, the slowness of approach to equilibrium.

* Garner reports a value of 37 for the initial heat of adsorption of oxygen on oxidised Cr_2O_3 at room temperature (Trapnell, "Chemisorption," Butterworths, 1955, p. 142).

In order to account for oxygen exchange with the whole surface, although adsorption occurs on only a small fraction, it is evident that either the adsorbed oxygen (O^-_{ads}) or the defects promoting adsorption are mobile in the surface. In the light of present knowledge it is not possible to say for certain which species is the more mobile; certainly above ~430° in the case of Cr_2O_3 the mobility of one species becomes rate-determining in the exchange (Fig. 1).

Some evidence pointing to distinctly limited mobility of adsorbed oxygen on NiO at temperatures rather lower than those used in the exchange–equilibration experiments (Fig. 1) was obtained as follows: 10 g. were outgassed overnight at 540°, isolated, cooled to 200°, and exposed for 10 min. at this temperature to 2 cm. of the non-equilibrated oxygen mixture. The gas left unadsorbed was recovered by Töpler pump, and the quantity adsorbed determined. The oxide was pumped for 30 sec. and then isolated from the back line and connected directly to the ionisation region of the mass spectrometer, by-passing the leak, so that all gas evolved from the oxide passed through the ionisation region and was analysed for masses 32, 34, and 36. There was no appreciable oxygen pressure over the oxide at 200°, and the temperature was raised fairly quickly in stages. Evolution of oxygen began at 220°, and was sufficient for analysis at 250°, 6 min. after the commencement of heating and 21 min. from the first adsorption; 3 min. later, at 300°, the gas evolved contained 4·8% of ^{18}O and *was not equilibrated*. Had the adsorbed gas exchanged with all the available oxide surface (the n_s value of ~10^{20} atoms $g.^{-1}$ obtained in higher-temperature exchange experiments being used) the ^{18}O content of the gas evolved should have been well below 0·30%: the value of 4·8% corresponds to exchange with 0·26% of the surface, or approximately two surface oxygen atoms exchanged for every one adsorbed (~$1·8 \times 10^{18}$ O atoms adsorbed; ~$3·8 \times 10^{18}$ O atoms in the surface suffered exchange). This experiment demonstrates clearly that at 250—300° the adsorbed oxygen is only able to exchange with (on the average) two nearest neighbour surface oxygen ions; there is no surface mobility of adsorbed gas leading to equilibration, which indicates that somewhere in the 90° temperature range between the exchange–equilibration reactions of Fig. 1 and this experiment it should be possible to separate the exchange and the equilibration reactions.

A similar experiment in which the gas was adsorbed at 105° on Cr_2O_3 showed that, at ~300°, 40 min. after the adsorption had started and 20 min. after heating of the oxide was begun, the gas first evolved had undergone complete exchange and equilibration with the whole oxide surface. This result is not surprising since the exchange–equilibration reaction is of measurable speed around 300° (cf. Fig. 1): in the case of Cr_2O_3, therefore, the adsorbed oxygen is held too tenaciously at lower temperatures to permit this method of studying surface mobility.

The reason for the rate of oxygen chemisorption on these oxides obeying Elovich's equation (1) is uncertain. This relation may be derived in at least three ways: (1) assume a uniform surface, with interaction between the adsorbed molecules or atoms; (2) assume a non-uniform surface (these two cases are mentioned by Trapnell, *op. cit.*, p. 104); (3) assume a uniform semiconducting surface, with charge transfer between the surface and adsorbed gas, leading to the formation of an electrical double layer at the interface. Case (3) has been discussed in detail by Engel and Hauffe (*Z. Elektrochem.*, 1952, **56**, 366; 1953, **57**, 762; see also Aigrain and Dugas, *ibid.*, 1952, **56**, 363) who call it "the boundary-layer theory" ("die Randschichttheorie") of chemisorption: they have also applied their equations to certain reactions catalysed by oxides and to the rates of oxidation of metals under conditions where the simple Wagner mechanism does not apply. Engel and Hauffe (*loc. cit.*, 1953, p. 773) have investigated the kinetics of adsorption of oxygen on NiO from room temperature to 700° and find that Elovich's equation is obeyed, although below 300° the plots of q against log $(t + t_0)$ show a discontinuity in every case, which they attribute to the presence of two processes, chemisorption and lattice incorporation, the former being the slow process at 300° and above. They found it necessary to put $t_0 \approx 60$—220 sec., and suggest that E_0, the activation energy of the adsorption at zero coverage, is about 11—12 kcal. $mole^{-1}$; the B.E.T. area of their sample, determined with NiO at −78°, was 61 $m.^2$, presumably measured

on the 62·9 g. of oxide used for the oxygen work, or about 1 m.^{2} g.$^{-1}$. It is satisfactory that our observations agree with those of Engel and Hauffe, insofar as the Elovich equation is concerned; the fact that we found E_0 and t_0 both ≈ 0 whereas the earlier workers did not may be due to differences in preparation. It appears that Engel and Hauffe's oxide was of much lower specific surface than ours, which would indicate a greater degree of sintering leading to a more uniform surface. We believe that the mechanism of oxygen adsorption on semiconducting oxides is due to a combination of cases (2) and (3), so that a sample with a highly non-uniform surface might well have $E_0 \approx 0$, whereas a well-sintered specimen may need an activation energy before appreciable quantities of oxygen are adsorbed. The accuracy of our adsorption experiments is not such (owing mainly to the nature of Elovich's equation) as to exclude the possibility in our case of $E_0 \approx 3$ kcal. mole^{-1}; also, the method whereby Engel and Hauffe arrive at a value of 11—12 is only approximate.

The presence of an electrical double layer on the oxide surface when oxygen is adsorbed is evident from the semiconductivity experiments, while some degree of non-uniformity is inevitable in oxide preparations of this type. Other oxides used by us, notably those of zinc and magnesium, possess a non-uniformity of surface which is readily demonstrated by the regular increase of n_s with the temperature of the exchange reaction, but, curiously, only nickel oxide, of the three oxides examined here, shows this effect over the temperature ranges studied. Some experiments on the mechanism of the reactions $2N_2O \longrightarrow 2N_2 + O_2$ and $2CO + O_2 \longrightarrow 2CO_2$, catalysed by these oxides, have shown, by use of ^{18}O, clear evidence of heterogeneity of surface in the case of NiO (Winter, unpublished work). Heterogeneity could probably be demonstrated also by oxygen-exchange reactions carried out at lower temperatures than those used in the present work.

The present results, together with those presented in Parts III—V (*locc. cit.*), demonstrate the rather surprising diversity in detail of behaviour towards oxygen of metallic oxides, and show how complicated may be the considerations controlling catalytic activity and electrical conductivity. The five oxides so far studied in detail comprise ZnO and Fe_2O_3 (both *n*-type conductors), NiO and Cr_2O_3 (*p*-type), and MgO [described as an insulator, but cf. Mansfield (*Proc. Phys. Soc.*, 1953, **66**, *B*, 612) and Lenpicki (*ibid.*, p. 281) who, using single crystals, examined the conductivity and thermoelectric power of MgO and concluded that it is a defect semiconductor containing excess of oxygen]: no two of these behave in exactly the same way, although the same basic reactions of dissociative chemisorption, surface migration, exchange, recombination and desorption of oxygen are undergone by each.

Finally, it is of interest to compare the surface areas deduced for these three oxides from the various studies reported here: Cr_2O_3 (A); B.E.T. (N_2) area of 30 m.^{2} g.$^{-1}$ corresponds to a calculated n_s of $\sim 3 \times 10^{20}$ atoms of oxygen g.$^{-1}$, a random exposure of crystalline faces being assumed; n_s observed was about $1{\cdot}8 \times 10^{20}$ atoms g.$^{-1}$. Cr_2O_3 (B); B.E.T. area 14·2 m.^{2} g.$^{-1}$ corresponding to n_s (calc.) of $1{\cdot}4 \times 10^{20}$ atoms g.$^{-1}$; n_s (obs.) $\approx 8 \times 10^{19}$ atoms g.$^{-1}$.

Similarly for NiO (in units of atoms g.$^{-1}$); B.E.T. $\approxeq 7 \times 10^{19}$; n_s (obs.) $\approx 9 \times 10^{19}$. For Fe_2O_3; B.E.T. $\approxeq 5 \times 10^{20}$ atoms per g. of oxygen, or $3{\cdot}3 \times 10^{20}$ per g. of iron; n_s (obs.) $= 6{\cdot}5 \times 10^{20}$ of oxygen; n_s deduced from the adsorption isotherm for iron from solution, $5{\cdot}3 \times 10^{20}$ of iron.

In view of the three widely differing techniques used, involving a temperature range of some 650°, the agreement is remarkable.

Certain of the results given for Cr_2O_3 (A) were obtained with the help of Dr. G. Houghton at Imperial College; I am also indebted to colleagues here for the B.E.T. measurements.

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Aryl-2-halogenoalkylamines. Part XV. Some Cationic and Basically Substituted Aryl Compounds.*

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The preparation of some *p*-di-(2-chloroethyl)aminobenzene derivatives with side chains carrying basic and cationic groups is described.

In continuation of work described in Part XII (*J.*, 1953, 2386) which aimed at obtaining aryl-2-halogenoalkylamines of more selective action on neoplasms by incorporating into the molecule substituents which would modify the physical properties, a series of compounds possessing basic and cationic side-chains has now been prepared. The first group of compounds has the general formula (I) whilst the cationic derivatives are trimethylammonium iodides of general formula (II).

(I) $(Cl\cdot CH_2\cdot CH_2)_2N\cdot C_6H_4\cdot[CH_2]_n\cdot NR'R$ $(Cl\cdot CH_2\cdot CH_2)_2N\cdot C_6H_4\cdot[CH_2]_n\cdot NMe_3^+)I^-$ (II)

The *p*-phenylenediamine derivative (I; $n = 0$, $R = R' = H$) was described in Part II (*J.*, 1949, 1972); the preparation of its *NN*-dimethyl derivative (I; $n = 0$, $R = R' = Me$) and the related trimethylammonium iodide (II; $n = 0$) is here reported.

p-Di-(2-chloroethyl)aminobenzylamine (I; $n = 1$, $R = R' = H$) was obtained by hydrogenation of the oxime of *p*-di-(2-chloroethyl)aminobenzaldehyde over a platinum catalyst; it was characterised as the monohydrochloride. Catalytic hydrogenation over Raney nickel of the Schiff's base obtained by condensing *p*-di-(2-chloroethyl)aminobenzaldehyde with methylamine afforded *p*-di-(2-chloroethyl)aminobenzylmethylamine (I; $n = 1$, $R = Me$, $R' = H$) and this on treatment with methyl iodide yielded the quaternary iodide (II; $n = 1$).

Nitration of *N*-phenethylsuccinimide gave the *p*-nitro-derivative which on hydrogenation over palladium–calcium carbonate afforded *N*-*p*-aminophenethylsuccinimide. This was converted into the di-(2-hydroxyethyl)amino- and di-(2-chloroethyl)amino-derivatives by the usual methods. Hydrolysis of the last compound by hot concentrated hydrochloric acid gave *p*-di-(2-chloroethyl)aminophenethylamine (I; $n = 2$, $R = R' = H$) which was isolated as the dihydrochloride monohydrate. The dichloroethyl derivative (I; $n = 2$, $R = R' = H$) was also prepared by an alternative route whereby *N*-*p*-nitrophenethylphthalimide formed the starting material and the aliphatic amino-group was throughout protected by the phthaloyl group. Somewhat better yields were obtained by this method.

On treatment of *N*-benzylidene-*p*-nitrophenethylamine with methyl iodide at 100°, a product was obtained which with hot acetic anhydride afforded *N*-acetyl-*N*-*p*-nitrophenethylmethylamine. This nitro-compound was hydrogenated over Raney nickel and the resultant *p*-amino-amide was converted into the di-(2-chloroethyl)amino-derivative in the usual manner. Removal of the acetyl group by acid gave *N*-[*p*-di-(2-chloroethyl)-aminophenethyl]methylamine (I; $n = 2$, $R = Me$, $R' = H$) which was characterised as the dihydrochloride.

p-Nitrophenethylamine yielded the *NN*-dimethyl derivative when treated with formaldehyde and formic acid. The *p*-amino-compound obtained by hydrogenation of this was converted successively into the *p*-di-(2-hydroxyethyl)amino- and the *p*-di-(2-chloroethyl)amino-compound (I; $n = 2$, $R = R' = Me$). The latter yielded the trimethylammonium iodide (II; $n = 2$).

Model experiments established that 2-*p*-acetamidophenoxyethyl bromide (III; $R = NHAc$) readily combined with trimethylamine, under conditions too mild for the reaction of a chloroethylarylamino-group, giving the quaternary salt (IV; $R = NHAc$). 2-*p*-Di-(2-hydroxyethyl)aminophenoxyethyl bromide [III; $R = N(CH_2\cdot CH_2\cdot OH)_2$]

* Part XIV, *J.*, 1955, 3110.

similarly gave *N*-[2-*p*-di-(2-hydroxyethyl)aminophenoxyethyl]trimethylammonium bromide [IV; R = $N(CH_2 \cdot CH_2 \cdot OH)_2$]. *N*-[2-*p*-Di-(2-chloroethyl)aminophenoxyethyl]-trimethylammonium bromide [IV; R = $N(CH_2 \cdot CH_2Cl)_2$] was not obtained by the action of phosphoryl chloride on the di(hydroxyethyl)amino-salt [IV; R = $N(CH_2 \cdot CH_2 \cdot OH)_2$] but was readily prepared from 2-*p*-di-(2-chloroethyl)aminophenoxyethyl bromide [III;

$R \cdot C_6H_4 \cdot O \cdot CH_2 \cdot CH_2Br$ (III) $\quad R \cdot C_6H_4 \cdot O \cdot CH_2 \cdot CH_2 \cdot NMe_3^+\}Br^-$ (IV) $\quad (X \cdot CH_2 \cdot CH_2)_2N \cdot C_6H_4 \cdot O \cdot CH_2 \cdot CH_2 \cdot NEt_2$ (V)

R = $N(CH_2 \cdot CH_2Cl)_2$] which was in turn derived from the di(hydroxyethyl) analogue [III; R = $N(CH_2 \cdot CH_2 \cdot OH)_2$]. The quaternary iodide was similarly prepared from the phenoxyethyl iodide. *NN*-Diethyl-*N*-[2-*p*-di-(2-hydroxyethyl)aminophenoxyethyl]-amine (V; X = OH), obtained by the action of diethylamine on the phenoxyethyl bromide, was readily converted into the di-(2-chloroethyl)amino-derivative (V; X = Cl).

Preliminary biological results indicate that whereas the primary amines (I; $n = 0$ and 2, R = R′ = H) are effective tumour-growth inhibitors, the tertiary amine (I; $n = 2$, R = R′ = Me) and the quaternary salts (II; $n = 2$) and [IV; R = $N(CH_2 \cdot CH_2Cl)_2$] are ineffective at the dose levels so far employed. This suggests that the un-ionised form of the amines is the active species but that conclusion is not supported by the dissociation constants of the series (I; $n = 2$). The pK_a's of the primary, secondary, and tertiary amines in this series (determined by potentiometric titration in water) are 9·7, 9·9, and 8·9 respectively. This indicates that a higher proportion of the active primary amine than of the inactive tertiary amine is in the cationic form at physiological pH.

It has not been possible to obtain rates of hydrolysis of the new compounds which can be directly compared with rates given in earlier Parts of this series, owing, in the case of the amines, to the instability (probably polymerisation) of the free bases when liberated from the hydrochlorides in aqueous solutions. The hydrolysis rates of the quarternary salts will be greatly influenced by the initial presence of the halide ions (cf. Part III, *J.*, 1949, 2589). The bromide [IV; R = $N(CH_2 \cdot CH_2Cl)_2$] and the corresponding iodide are hydrolysed to the extent of 35% and 30% respectively in 30 minutes under standard conditions.

A more complete account of the biological activity of the new compounds together with further physical measurements will be given elsewhere.

Experimental

NN-*Dimethyl*-p-*di*-(2-*chloroethyl*)*aminoaniline Dihydrochloride*.—A solution of *p*-di-(2-chloroethyl)aminoaniline hydrochloride (1·7 g.) and formaldehyde (5 ml. of 36% solution) in ethanol (40 ml.) containing platinum oxide (50 mg.) was shaken in an atmosphere of hydrogen for 12 hr. The filtered solution was saturated with anhydrous hydrogen chloride and then evaporated under reduced pressure. The *dihydrochloride* thus obtained formed prisms, m. p. 186—188°, from ether–ethanol (Found: C, 43·1; H, 6·2; N, 8·5. $C_{12}H_{18}N_2Cl_2,2HCl$ requires C, 43·1; H, 6·0; N, 8·4%).

NNN-*Trimethyl*-p-*di*-(2-*chloroethyl*)*aminoanilinium Iodide*.—*p*-Di-(2-chloroethyl)aminoaniline hydrochloride (7 g.), methyl iodide (12 ml.), and sodium carbonate (6 g.) in ethanol (60 ml.) were heated on a steam-bath for 2 hr. The quaternary *iodide* which separated when the filtered solution was cooled formed plates, m. p. 145—146°, from ethanol (Found: C, 38·9; H, 5·5; N, 7·0. $C_{13}H_{21}N_2Cl_2I$ requires C, 38·7; H, 5·2; N, 7·0%).

p-*Di*-(2-*chloroethyl*)*aminobenzylamine Hydrochloride*.—Hydroxylamine hydrochloride (14·3 g.) and sodium acetate (16·6 g.) in water (50 ml.) were added to *p*-di-(2-chloroethyl)aminobenzaldehyde (Anker and Cook, *J.*, 1944, 489) (25 g.) in methanol (300 ml.). p-*Di*-(2-*chloroethyl*)-*aminobenzaldoxime* which separated overnight formed prisms, m. p. 104—106°, from benzene–light petroleum (b. p. 40—60°) (Found: C, 50·5; H, 5·6; N, 10·5. $C_{11}H_{14}ON_2Cl_2$ requires C, 50·6; H, 5·4; N, 10·7%). A solution of the oxime (1·9 g.) in methanol (50 ml.) was shaken in hydrogen over a platinum catalyst. The filtered solution was saturated with dry hydrogen chloride and diluted with dry ether. The p-*di*-(2-*chloroethyl*)*aminobenzylamine hydrochloride* (1·2 g.) thus obtained formed prisms, m. p. 218—221°, from ether–methanol (Found: C, 46·7; H, 6·0; N, 9·6. $C_{11}H_{17}N_2Cl_3$ requires C, 46·6; H, 6·0; N, 9·9%).

N-p-*Di*-(2-*chloroethyl*)*aminobenzylmethylamine Dihydrochloride*.—A mixture of ethanolic methylamine (1·2 ml.; 33% w/v) and *p*-di-(2-chloroethyl)aminobenzaldehyde (2·5 g.) in ethanol (30 ml.) was shaken at room temperature for 4 hr. Next day the filtered solution was evaporated under reduced pressure and the residual *N*-*p*-di-(2-chloroethyl)aminobenzylidenemethylamine was characterised by the preparation of its *picrate*, prisms, m. p. 164° (after sintering at 147°) (from ethanol) (Found: C, 44·6; H, 4·1; N, 14·0. $C_{18}H_{19}O_7N_5Cl_2$ requires C, 44·3; H, 3·9; N, 14·3%). The Schiff's base (1·8 g.), without further purification, was hydrogenated in ethanol (50 ml.) over Raney nickel. Dry hydrogen chloride was passed into the filtered solution which on dilution with dry ether afforded N-p-*di*-(2-*chloroethyl*)*aminobenzylmethylamine dihydrochloride* (0·7 g.), prisms, m. p. 165—170° (decomp.) (from ether–ethanol) (Found: C, 43·2; H, 6·5; N, 8·2. $C_{12}H_{18}N_2Cl_2,2HCl$ requires C, 43·1; H, 6·1; N, 8·4%).

N-p-*Di*-(2-*chloroethyl*)*aminobenzyltrimethylammonium Iodide*.—A mixture of the above product (0·17 g.), methyl iodide (2 ml.), and sodium carbonate (0·5 g.) in ethanol (10 ml.) was kept at room temperature for 48 hr. On dilution of the filtered solution with ether the quaternary *salt*, which formed prisms, m. p. 164—167°, from methanol, was obtained (Found: C, 40·5; H, 5·9; I, 6·4. $C_{14}H_{23}N_2Cl_2I$ requires C, 40·3; H, 5·6; N, 6·7%).

N-p-*Aminophenethylsuccinimide*.—*N*-Phenethylsuccinimide (20 g.) was added to concentrated nitric acid (100 ml.), and the stirred mixture was kept at 20° for 5 hr. The solid which separated when the mixture was poured on crushed ice was extracted with *cyclo*hexane, and the residue was crystallised from benzene. The p-*nitro*-derivative formed prisms, m. p. 125—126° (Found: C, 58·1; H, 4·9; N, 11·5. $C_{12}H_{12}O_4N_2$ requires C, 58·1; H, 4·8; N, 11·3%). The p-*amino*-derivative obtained by hydrogenation of the nitro-compound over palladium–calcium carbonate in ethanol–ethyl acetate formed plates, m. p. 198°, from ethyl acetate (Found: C, 65·7; H, 6·6; N, 12·8. $C_{12}H_{14}O_2N_2$ requires C, 65·9; H, 6·5; N, 12·8%).

p-*Di*-(2-*chloroethyl*)*aminophenethylamine*.—Ethylene oxide (5 ml.) was added to *N*-*p*-aminophenethylsuccinimide (2 g.) dissolved in dilute acetic acid (20 ml., 50% v/v), and the mixture was stirred at 20°. After 18 hr. the product was isolated in the usual manner. N-p-*Di*-(2-*hydroxyethyl*)*aminophenethylsuccinimide* (yield, 0·7 g.) formed plates, m. p. 161—162°, from benzene (Found: C, 62·4; H, 7·3; N, 8·9. $C_{16}H_{22}O_4N_2$ requires C, 62·7; H, 7·2; N, 9·1%).

On treatment with phosphorus oxychloride in benzene solution this compound was converted into the *di*-(2-*chloroethyl*)*amino*-derivative, which formed platelets, m. p. 77°, from benzene–light petroleum (b. p. 60—80°) (Found: C, 56·0; H, 6·0; N, 8·4; Cl, 20·5. $C_{16}H_{20}O_2N_2Cl_2$ requires C, 56·0; H, 5·9; N, 8·2; Cl, 20·7%). The di-(2-chloroethyl)amino-derivative (0·7 g.) was heated for 2 hr. with concentrated hydrochloric acid (4 ml.), and then the solution was evaporated to dryness under reduced pressure. The solid residue, crystallised from methanol–ethyl acetate, gave p-*di*-(2-*chloroethyl*)*aminophenethylamine dihydrochloride monohydrate*, m. p. 163° (Found: C, 40·9; H, 6·3; N, 8·0; Cl, 40·1. $C_{12}H_{18}N_2Cl_2,2HCl,H_2O$ requires C, 40·9; H, 6·3; N, 8·0; Cl, 40·3%).

N-p-*Aminophenethylphthalimide*.—Phthalic anhydride (14 g.) was added to 2-*p*-nitrophenethylamine (16 g.) dissolved in benzene (30 ml.) and the mixture was shaken at room temperature for 2 hr. The solid which separated was crystallised from pentyl alcohol, giving N-p-*nitrophenethylphthalimide* (14 g.), as plates, m. p. 205—206° (Found: C, 64·7; H, 4·3; $C_{16}H_{12}O_4N_2$ requires C, 64·8; H, 4·1%).

Hydrogenation of the *p*-nitro-compound over palladium–calcium carbonate in methanol afforded N-p-*aminophenethylphthalimide* (9·0 g.), which formed cream-coloured needles, m. p. 162°, from benzene (Found: C, 72·2; H, 5·3. $C_{16}H_{14}O_2N_2$ requires C, 72·1; H, 5·4%).

N-p-*Di*-(2-*chloroethyl*)*aminophenethylphthalimide*.—The *p*-amino-compound (2·0 g.) was hydroxyethylated in the usual manner, giving the *di*-(2-*hydroxyethyl*)*amino*-derivative (1·1 g.), yellow needles, m. p. 140° (from benzene) (Found: 67·8; H, 6·4. $C_{20}H_{22}O_4N_2$ requires C, 67·8; H, 6·3%). This was converted into the corresponding *di*-(2-*chloroethyl*)*amino*-derivative (0·5 g.), which formed needles, m. p. 107—109°, from pentane (Found: C, 61·5; H, 5·3. $C_{20}H_{20}O_2N_2Cl_2$ requires C, 61·4; H, 5·2%). The *N*-*p*-di-(2-chloroethyl)aminophenethyl)-phthalimide (400 mg.) was heated under reflux for 3 hr. with concentrated hydrochloric acid (20 ml.). After removal of the phthalic acid which separated from the cooled solution the filtrate was evaporated under reduced pressure, the dihydrochloride monohydrate, m. p. 163° (230 mg.), described above, being obtained.

N-*Acetyl*-N-p-*nitrophenethylmethylamine*.—N-*Benzylidene*-p-*nitrophenethylamine* (23·2 g.), prepared by mixing *p*-nitrophenethylamine (16·8 g.) and benzaldehyde (10·6 g.), formed needles, m. p. 77°, from light petroleum (b. p. 60—80°) (Found: C, 70·8; H, 5·6; N, 11·5. $C_{15}H_{14}O_2N_2$ requires C, 70·8; H, 5·5; N, 11·0%). This derivative (5·8 g.) and methyl iodide

(2·8 g.) were heated together in a sealed tube at 100° for 5 hr. The product was dissolved in hot aqueous ethanol (95%; 20 ml.) and on the addition of ether (200 ml.) a hydriodide (5·2 g.), m. p. 145°, was precipitated. Heating the free base (obtained by treating the hydriodide with 2N-sodium carbonate) with acetic anhydride (4 vols.) gave *N-acetyl-N-nitrophenethylmethylamine*, m. p. 101°, needles (from *cyclo*hexane) (Found: C, 59·7; H, 6·4; N, 13·0. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·4; N, 12·6%).

N-*Acetyl*-N-p-*aminophenethylmethylamine*.—The nitro-compound was hydrogenated in methanol over palladium–calcium carbonate. The *p*-amino-compound thus obtained formed a *hydrochloride*, m. p. 184°, plates from ether–methanol (Found: C, 50·1; H, 7·0; Cl, 26·0. $C_{11}H_{16}ON_2,2HCl$ requires C, 49·8; H, 6·8; Cl, 26·7%).

N-*Acetyl*-N-[p-*di*-(2-*chloroethyl*)*aminophenethyl*]*methylamine*.—The above amine (10 g.) was dissolved in 2N-acetic acid (100 ml.) containing ethylene oxide (10 ml.) and kept at room temperature overnight. The excess of ethylene oxide was then removed under reduced pressure and the product was extracted from the aqueous solution with ether after neutralisation with aqueous ammonia. The non-crystalline *N*-acetyl-*N*-[*p*-di-(2-hydroxyethyl)aminophenethyl]-methylamine (5 g.), dissolved in dry benzene (50 ml.), was heated under reflux with phosphorus oxychloride (10 ml.) for 30 min., after which the mixture was evaporated under reduced pressure. Concentrated hydrochloric acid (20 ml.) was added, the mixture was heated for 30 min. and then cooled, and the pH adjusted to 7 by the addition of aqueous 2N-ammonia. The liberated N-*acetyl*-N-[p-*di*-(2-*chloroethyl*)*aminophenethyl*]*methylamine* formed plates, m. p. 111°, from light petroleum (b. p. 60—80°) (Found: C, 56·9; H, 7·2. $C_{15}H_{22}ON_2Cl_2$ requires C, 56·8; H, 7·0%).

N-[p-*Di*-(2-*chloroethyl*)*aminophenethyl*]*methylamine*.—The preceding *N*-acetyl compound was (0·5 g.) heated under reflux with concentrated hydrochloric acid (10 ml.) for 3 hr. and then the solution was evaporated to dryness under reduced pressure (0·7 g.). Crystallising the residue from ether–ethanol gave the N-[p-*di*-(2-*chloroethyl*)*aminophenethyl*]*methylamine dihydrochloride* as plates, m. p. 196° (Found: C, 45·0; H, 6·6; N, 8·0; Cl, 39·3. $C_{13}H_{20}N_2Cl_2,2HCl$ requires C, 44·8; H, 6·4; N, 8·1; Cl, 40·7%).

N-p-*Aminophenethyldimethylamine*.—A mixture of *p*-nitrophenethylamine (8 g.), 90% formic acid (12 g.), and 35% formaldehyde (12 ml.) was kept at 40° until evolution of gas began and then left at room temperature for 24 hr. After addition of concentrated hydrochloric acid (60 ml.) the mixture was steam-distilled in order to remove formic acid and formaldehyde. Excess of sodium hydroxide was then added and the mixture again steam-distilled. The distillate, after addition of solid potassium hydroxide, was extracted with ether, and after evaporation of the ether the residue was passed in pentane down a short column of alumina. The oily main product (3 g.) on elution with pentane formed a picrate, m. p. 162° (prisms from benzene). The picrate of *p*-nitrophenethyldimethylamine prepared by Goss, Hanhart, and Ingold (*J.*, 1926, 256) by nitration of phenethyldimethylamine had the same m. p.

Catalytic hydrogenation of the *p*-nitro-compound (3 g.) over palladium–calcium carbonate in methanol gave 2-*p*-aminophenethyldimethylamine (2·5 g.), as an oil which formed a *picrate*, m. p. 150° (prisms from ethanol–benzene) (Found: C, 49·0; H, 4·8; N, 17·7. $C_{16}H_{19}O_7N_5$ requires C, 48·9; H, 4·8; N, 17·8%).

N-[p-*Di*-(2-*chloroethyl*)*aminophenethyl*]*dimethylamine*.—The di-(2-hydroxyethyl)amino-derivative (1·5 g.) obtained by treating the above *p*-amino-compound with ethylene oxide in the usual manner was heated with thionyl chloride (2 ml.) in benzene (20 ml.) for 1 hr. The solid which separated was collected and dissolved in water. Ammonia was added and the mixture was extracted with ether–benzene. The dried extract was evaporated and the residue was dissolved in pentane and passed down a short column of activated alumina. The eluates afforded the *di*-(2-*chloroethyl*)*amino*-compound as a light yellow oil (Found: C, 58·1; H, 7·5. $C_{14}H_{22}N_2Cl_2$ requires C, 58·2; H, 7·3%).

Heating this with an equal weight of methyl iodide in benzene for 5 min. gave the corresponding *trimethylammonium iodide*, m. p. 148—149° (from water) (Found: N, 6·3; total halogen, 45·3. $C_{15}H_{25}N_2Cl_2I$ requires N, 6·5; total halogen, 45·9%).

N-(2-p-*Acetamidophenoxyethyl*)*trimethylammonium Bromide*.—2-*p*-Acetamidophenoxyethyl bromide (200 mg.) and trimethylamine (2 ml.) in methanol (15 ml.) were heated in a sealed tube at 100° for 1 hr. On cooling to −10° the solution deposited a solid which was collected and washed with ether. The quaternary *bromide* had m. p. 235°, when precipitated from methanol by ether (Found: 48·8; H, 6·7; N, 8·8. $C_{13}H_{21}O_2N_2Br$ requires C, 49·2; H, 6·7; N, 8·8%).

N-[2-p-*Di*-(2-*hydroxyethyl*)*aminophenoxyethyl*]*trimethylammonium Bromide*.—A solution of 2-*p*-di-(2-hydroxyethyl)aminophenoxyethyl bromide (500 mg.) in methanol (6 ml.) containing

trimethylamine (3 ml.) was kept at room temperature for 48 hr. The oil which separated on addition of ether yielded a solid when rubbed with acetone. The quaternary *bromide* thus obtained formed small prisms, m. p. 112—113°, from ether–methanol (Found : C, 49·6; H, 7·6; N, 7·6. $C_{15}H_{27}O_3N_2Br$ requires C, 49·6; H, 7·5; N, 7·7%).

2-Di-(2-chloroethyl)aminophenoxyethyl Bromide and Iodide.—*p*-Di-(2-hydroxyethyl)aminophenoxyethyl bromide (5 g.) was heated for 2 hr. with phosphorus oxychloride (5 ml.) in dry benzene (20 ml.). The cooled solution was poured on ice, and the dried benzene layer was passed through activated alumina. The eluates contained 2-p-*di-(2-chloroethyl)aminophenoxyethyl bromide* (2·6 g.) which formed prisms, m. p. 79—80°, from light petroleum (b. p. 40—60°) (Found : C, 42·5; H, 4·9; N, 4·2. $C_{12}H_{16}ONCl_2Br$ requires C, 42·3; H, 4·7; N, 4·1%).

The bromide (340 mg.) was heated for 2 hr. in a solution of sodium iodide (200 mg.) in acetone (5 ml.). The *iodide* thus obtained formed needles, m. p. 75°, from light petroleum (b. p. 40—60°) (Found : C, 37·5; H, 4·4. $C_{12}H_{16}ONCl_2I$ requires C, 37·1; H, 4·2%).

N-[2-p-*Di-(2-chloroethyl)aminophenoxyethyl]trimethylammonium bromide* which formed plates, m. p. 114—116°, from methanol (Found : C, 44·8; H, 6·4; N, 6·9. $C_{15}H_{25}ON_2Cl_2Br$ requires C, 45·0; H, 6·3; N, 7·0%) and the corresponding *iodide*, needles, m. p. 139°, from ether–methanol (Found : C, 39·8; H, 6·1; N, 6·0. $C_{15}H_{25}ON_2Cl_2I$ requires C, 40·3; H, 5·6; N, 6·3%) were similarly prepared from the appropriate halides which are described above.

N-[2-p-*Di-(2-hydroxyethyl)aminophenoxyethyl]diethylamine.*—2-*p*-Di-(2-hydroxyethyl)aminophenoxyethyl bromide (5 g.) and diethylamine (5 ml.) in benzene (50 ml.) were heated under reflux for 17 hr. The solution was then washed with 2N-ammonia and water, dried, and evaporated. The oily diamine formed a *dipicrate*, m. p. 159—160°, as prisms from benzene–methanol (Found : C, 45·1; H, 5·0; N, 14·8. $C_{28}H_{34}O_{17}N_8$ requires C, 44·6; H, 4·5; N, 14·8%).

N-[2-p-*Di-(2-chloroethyl)aminophenoxyethyl]diethylamine.*—The above diamine (5 g.) was heated for 1 hr. in a solution of phosphorus oxychloride (5 ml.) in benzene (15 ml.). The solution was then evaporated under reduced pressure and this process was repeated twice after the addition of dry benzene (25 ml.). The residue was heated for 20 min. with concentrated hydrochloric acid (20 ml.), and the cooled solution was saturated with sodium acetate. The solution was extracted with chloroform and the aqueous layer was neutralised with sodium carbonate and again extracted. The combined chloroform extracts were dried and evaporated and a solution of the residue in light petroleum (b. p. 60—80°) was passed through alumina. The *di-(2-chloroethyl)amino*-compound was obtained as a straw-coloured oil (Found : N, 8·5; Cl, 21·6. $C_{16}H_{26}ON_2Cl_2$ requires N, 8·4; Cl, 21·2%). The diamine formed a *dihydrochloride*, prisms, m. p. 162—163°, from methanol–ether (Found : C, 46·9; H, 6·7; N, 7·1. $C_{16}H_{26}ON_2Cl_2,2HCl$ requires C, 47·3; H, 6·9; N, 6·9%) and a *dipicrate*, prisms, m. p. 119—121°, from benzene (Found : N, 14·2. $C_{28}H_{32}O_{15}N_8Cl_2$ requires N, 14·2%).

Potentiometric titration of the diamine indicated that the pK_a of the basic groups were 3·1 and 8·2.

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The Polarisation of Azobenzene as a Vapour.

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Modifications of previously used apparatus are described, making possible the taking of polarisation measurements up to temperatures of 340°. The total polarisation of azobenzene as a gas is found to be *ca.* 66 c.c.—a value of the order to be expected from the known molecular refraction, and one indicating that the atomic polarisation is about 9 c.c.

As azobenzene boils at 293° at ordinary pressures the thermostat and cell arrangements previously found satisfactory up to *ca.* 200° (cf. Le Fèvre and Russell, *Trans. Faraday Soc.*, 1947, **43**, 374; Le Fèvre, Ross, and Smythe, *J.*, 1950, 276; Le Fèvre, Mulley, and Smythe, *J.*, 1950, 290) required modification as follows.

Experimental

The gas cell has the dimensions given by Le Fèvre (" Dipole Moments," 3rd Edn., Methuen and Co. Ltd., London, 1953, p. 38), but instead of mercury-containing side-arms the emergent platinum leads are spot-welded to stout copper wires which pass through the roof of the oven. The lead from the central cylinder of the condenser is insulated by being threaded through Pyrex glass tubing, which in turn is surrounded by an earthed brass pipe which projects 1" above and below the case of the thermostat. If the angular coaxial-cable connection holding the cable from the oscillator were soldered directly to the top of the brass tube the plastic dielectric would be affected by heat. Therefore the connector is separated from the tube by three 1" vertical, thin, brass rods; this arrangement effectively shields the glass-insulated part of the lead. The second lead from the cell is brought out naked and soldered to the earthed outer edge of the cable connector.

The thermostat is constructed from a laboratory drying oven (internally 1' cube) lagged with two layers of 1/4" asbestos sheet on all six faces. Electrical heating elements are carried on asbestos boards on the left and right inner walls and the floor. The shaft of a fan stirrer, powered by an external motor, enters from underneath. The gas cell is supended from the (removable) centre of the roof by a thick brass rod to the bottom of which is screwed a " spider " upon which the cell rests. " Temperature smoothing " is effected by means of a massive aluminium cylinder, of external diameter 3·25", which completely surrounds the cell; the cell fits snugly into a cavity of diameter 2". To allow access to the cell, the aluminium block is split length-wise. The rear section is fixed independently of the cell to the roof and the front section is screwed to the rear section by wing nuts and bolts passing through ears. Accommodation for the gas-inlet tube of the cell is moulded in the aluminium halves. A bimetallic thermo-control is fitted through the front part of the roof; the temperature of the cell contents is read by a thermometer whose bulb is level with, and close to, the centre of the cell.

The gas-handling apparatus is indicated in the Figure. Items to the left of the manometer M_3 are used for the purification of the carbon dioxide or sulphur dioxide used as standard. Bulb *A* contains phosphoric oxide supported on glass-wool. The gas is distilled from its cylinder through *A* into trap *B*; traps *B* and *C* serve for the repeated cyclic distillation of the gas, which may be passed through *A* or not, as desired. Trap *D*, which is removable, serves for the tapping-off of the first and last fractions of the distillations. Trap *B* can also be removed, to make possible the introduction of drying agents, distillation from fresh phosphoric oxide being the most efficient. The bulbs *E* and *E'* contain glass-wool to prevent phosphoric oxide being carried through the apparatus when the liquid in the trap *B* bumps while boiling: after each gas-purification, these bulbs are cut out and washed.

The pressure of the gas is checked at all stages by connections to the manometers M_1 and M_2. The gas is finally collected in trap *C*, and is distilled into the gas-cell when required.

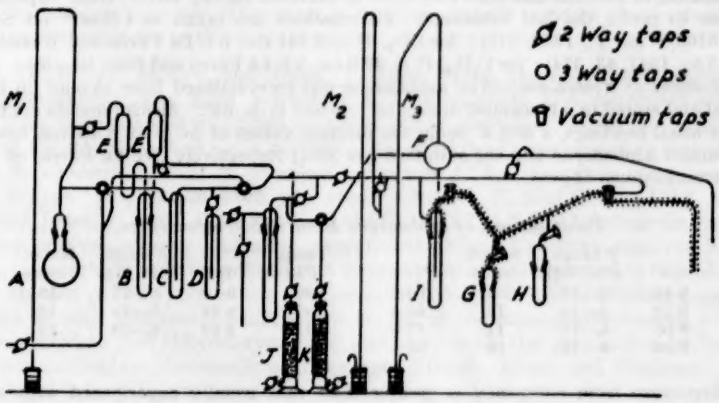
The remainder of the apparatus is provided for the handling of substances, which (melted if necessary) can be boiled in the tubes *G* and *H*. The glass tubing, taps, and ground-glass joints between the tubes and the cell are wound with Nichrome resistance wire (0·0285" diam.,

10 turns/in.). The heating system is supplied with current from a 240 v, 9 a, variable transformer set at 170—230 v, depending on the desired temperature. The liquid is first frozen in the tube *G* or *H*, the apparatus is evacuated, and, on melting, the liquid may be vapourised by heating it with a Bunsen burner. After measurement, the vapour is collected in the liquid-air trap *I*. The vacuum-taps in the high-temperature sections of the apparatus are lubricated with Silicone grease (Imperial Chemical Industries Limited). Even so, entrainment of the grease by the vapours at high tempertures necessitates the occasional dismantling, washing, and re-assembly of the hot-vapour handling system.

The manometer M_3 measures the pressure of air which, in the glass-diaphragm gauge to be described below, balances the pressure exerted by the vapour in the cell. The bulb *F* both increases the volume of the balancing system and acts as a splash-trap for mercury in the event of accidents to M_3.

The towers *J* and *K* serve to admit air (dried by $CaCl_2$ or P_2O_5) to the gas-handling and pressure-balancing systems, respectively.

For the applications now intended it is necessary to measure the pressure of a vapour at a high temperature, without allowing condensation to take place on cooler parts of the apparatus. The vapour must therefore be separated from the manometer on which the pressure readings are



taken. In addition, the pressure must be known with an accuracy of ±1 mm. Hg, and measurements must be possible over the ranges 0—760 mm. Hg and 20—300° or above. Speed of manipulation of the measuring device is important.

The small number of potentially useful devices has been reviewed by Partington (" Advanced Treatise on Physical Chemistry," London, 1949, Vol. I, p. 560). Eventually, a glass-diaphragm gauge of the type described by Lockspeiser (*J. Sci. Inst.*, 1930, **7**, 145), who used silica as the material, or by Klemenc (*J. Amer. Chem. Soc.*, 1925, **47**, 2173) was constructed and is part of the apparatus.

The vapour is confined inside a small (1"-diam.) glass bulb inside the thermostat and is connected to the outlet from the gas-cell. One side of the glass bulb, whose walls are extremely thin (*ca.* 0·1 mm.) has been carefully flattened by heating in a cool flame; this forms a diaphragm, tightly stretched across the decapitated bulb, which responds with a movement of 1—2 mm. at the centre to variations of the pressure difference between its two sides. Of over 200 diaphragms thus made, only two survived a pressure difference of 1 atm. at 200—300°.

The bulb is sealed by a ring-seal into the lower end of a glass cylinder, which projects through the roof of the oven and is connected to the bulb *F* and manometer M_3. The balancing pressure may be lowered by pumping or raised by admission of air through a phosphoric oxide tower.

A light metal spring rests on the upper surface of the diaphragm. In the equilibrium position, this spring just touches a rigidly supported platinum-wire point, making an electrical circuit which lights a small bulb fastened on the scale of M_3. The pressure reading is thus made whenever the light " goes on."

The pressure gauge is calibrated before each series of readings, *i.e.*, at every temperature, since electrical contact is not necessarily made when the known and the unknown pressure are

equal; a small difference usually exists. Calibration is easily achieved by admitting known pressures of air—measured on M_2—into the cell, and then observing on M_3 the value at which the bulb lights. The calibration also measures the consistency of the readings. Under the extreme condition of 320°, readings were consistent to within 3 mm., and the mean of four readings usually gave a value which was not altered much by further readings. Nevertheless, sudden changes in the calibration factor did occur in several runs at temperatures above 220°, and half-hourly re-calibrations are part of the measuring routine. The gauge cannot be used with the apparatus described at temperatures above 320°, which is thus the effective upper limit to the temperature of measurement. At this point the thermostat arrangements have been found usually to hold the cell temperature constant to 0·25°, though slow drifts of up to 1° per hour sometimes take place; these can easily be counterbalanced by manual adjustment of the regulator.

The whole apparatus has been in use for several years, measurements on 1 : 8-cineole (Freeman, Le Fèvre, and Maramba, *J.*, 1952, **1649**), methylene dibromide and bromoform (Buckingham and Le Fèvre, *J.*, 1953, **3432**), benzyl alcohol (Buckingham, Le Fèvre, and Holland, *J.*, 1954, **1646**), and various non-polar substances (Le Fèvre and Rao, *Australian J. Chem.*, 1954, **7**, 135; 1955, **8**, 39) being made with it. As standardising gases sulphur dioxide, carbon dioxide, or benzene has been employed at different times; lately, from experience, we have come to prefer the last substance. Polarisations are taken as follow: for SO_2, $P = 10{\cdot}9 + 16160/T$ (cf. *J.*, 1950, 276); for CO_2, $P = 7{\cdot}341$ c.c. (cf. Le Fèvre and Russell, *Trans. Faraday Soc.*, 1947, **43**, 374); for C_6H_6, $P = 27{\cdot}0$ c.c. (cf. Le Fèvre and Rao, *loc. cit.*).

Polarisations of Azobenzene.—The azobenzene was recrystallised from alcohol (in the dark) then dried and stored in a blackened desiccator; it had m. p. 68°. Measurements are tabulated under the usual headings, x and x' being the limiting values of $\Delta C/p$ as p approaches zero for the vapourised azobenzene and the standard gas (CO_2) respectively (see Le Fèvre, *op. cit.*, and other references given above).

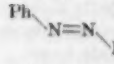
Polarisations of azobenzene at various temperatures.

Temp. (°K)	x/x'	p range (cm. Hg)	No. of obstns.	P (c.c.)	Temp. (°K)	x/x'	p range (cm. Hg)	No. of obstns.	P (c.c.)
509·4	9·48	5—11	9	69·2	569	9·10	5—17	19	66·8
513	9·32	3—14	16	68·4	587	9·48	3—19	17	69·6
529·5	9·16	4—17	11	67·3	611	8·91	6—23	18	65·4
541	9·06	6—19	16	66·5					

The departure from constancy is greater than that usually experienced with non-polar dielectrics at lower temperatures. Noting that our higher temperatures exceed those recorded by Coop and Sutton (*J.*, 1938, **1269**) by some 50°, we consider our results to be fairly satisfactory when judged against those shown by these authors for certain acetylacetone complexes (*e.g.*, of Cr, 127·5—133·7 c.c., or of Al, 129·3—132·8 c.c.). The mean, with standard variation, of the above seven determinations is therefore $67{\cdot}6 \pm 1{\cdot}5$ c.c.

Such a conclusion is in harmony with the $\infty(P_2)$ of 67 c.c. found in benzene as solvent by Hartley and Le Fèvre (*J.*, 1939, **531**). It is also compatible with the known refractivities (in c.c.) of azobenzene. These, determined on molten material or on solutions in various solvents, have ranged between $R_\alpha = 62{\cdot}28$ c.c. for the melt to $R_D = 65{\cdot}33$ in acetic acid (Duval, *Compt. rend.*, 1911, **153**, 875; Auwers and Heimke, *Ber.*, 1928, **61**, 1030; Auwers, *Ber.*, 1938, **71**, 611). The nearness of the above wave-lengths to absorption lines will invalidate the usual extrapolations to R_∞, but—noting that R_α or R_D is calculated from bond constants by Auwers (*loc. cit.*) as around 57 c.c.—we may infer that the atomic polarisation is about 10 c.c. (*i.e.*, roughly 17% of ${}_EP$).

That such an estimate is reasonable may be demonstrated as follows. Considering *trans*-azobenzene as the 4-point system inset, and applying parallel arguments to those used by Le Fèvre and Rao (*locc. cit.*), we compute ${}_AP$ as the sum of three terms due to stretching, in-plane bending, and twisting modes respectively:



$$ {}_AP = \frac{8\pi N e^2}{9k_1} + \frac{8\pi N\mu^2}{9k_2} + \frac{8\pi N\mu^2}{9k_\tau} $$

where e is the electronic charge, μ is the link moment μ_{Ph-N}, and k_1, k_2, or k_τ the appropriate force constants. The last are, of course, unknown for azobenzene. Their order of magnitude

being assumed to be $k_1 = 10^5$ dynes/cm., and k_3 or $k_\tau = 2 \cdot 10^{-12}$ ergs/radian^2, $_AP$ emerges—with $\mu = 2$ D (cf. Le Fèvre and Vine, *J.*, 1938, 431)—as around 7 c.c., to which *ca.* 2 c.c. may be added for the phenyl groups (Le Fèvre and Rao, *loc. cit.*), making 9 c.c. in all.

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The Synthesis of Sugars from Simpler Substances. Part IX. The Enzymic Synthesis of* 5 : 6-*Dideoxy*-D-threo*hexulose.*

By P. A. J. GORIN, L. HOUGH, and J. K. N. JONES.

[Reprint Order No. 6484.]

Propionaldehyde and D-fructose 1 : 6-diphosphate yield 5 : 6-dideoxy-D-*threo*hexulose in the presence of an enzyme preparation from peas which has aldolase activity. This result is in agreement with previous observations on the specificity of this enzyme system.

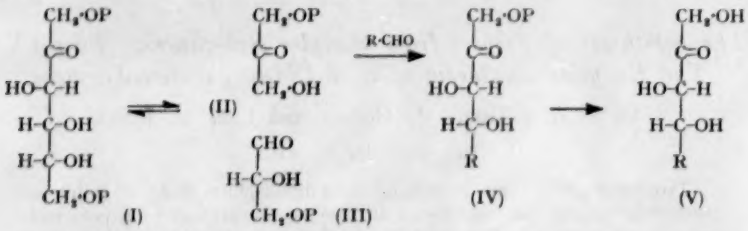
IN Part VII (Gorin, Hough, and Jones, *J.*, 1953, 2140), the enzymatic preparation of 5 : 6-dideoxy*threo*hexulose from D-fructose 1 : 6-diphosphate and propionaldehyde was noted. This hexulose was identified on paper chromatograms. Since conclusive identification of the sugar was lacking, a new preparation of the dideoxyhexulose was made. A mixture in aqueous solution of disodium D-fructose 1 : 6-diphosphate, propionaldehyde, and an enzyme preparation from pea seeds (Stumpf, *J. Biol Chem.*, **1948**, **176**, 233; Hough and Jones, *J.*, 1952, 4047) was kept at pH 6 for 22 hr. The solution was then heated to destroy enzyme activity and after precipitated protein had been removed by centrifugation, the resulting supernatant solution was evaporated. Extraction of the solid residue with hot acetone gave a syrup which, when examined on paper chromatograms, was shown to contain at least two components which moved at the rates corresponding to 5 : 6-dideoxy*threo*hexulose and dihydroxyacetone and gave with the *p*-anisidine hydrochloride and diphenylamine–trichloroacetic acid reagents (Hough, Jones, and Wadman, *J.*, 1950, 1702) corresponding colour reactions. The syrupy dideoxyhexulose was isolated by chromatography on sheets of filter paper (Flood, Hirst, and Jones, *J.*, 1948, 1679). Warming of the dideoxyhexulose with excess of phenylhydrazine acetate, gave in good yield a phenylosazone which had the same physical characteristics (m. p., mutarotation, and *X*-ray powder photograph) as authentic 5 : 6-dideoxy-D-*threo*hexose phenylosazone (Gorin, Hough, and Jones, *J.*, 1955, 2699). Under conditions whereby 1 mol. of D-xylose was oxidised by 0·94 mol. of sodium hypoiodite at pH 11·4 (Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289), the dideoxyhexulose consumed only 0·35 mol. of the reagent; 1 mol. of 5-deoxy-D-*threo*pentulose consumed under the same conditions 0·26 mol. of sodium hypoiodite (Gorin, Hough, and Jones, 1953, *loc. cit.*).

The formation of a 5 : 6-dideoxyhexulose with the D-*threo*-configuration at $C_{(3)}$ and $C_{(4)}$ is in accordance with our previous observations concerning the specificity of the pea-seed enzyme preparation, which contains, amongst other enzymes, aldolase(s ?), phosphatase, and triose phosphate isomerase (Stumpf, *loc. cit.*; Hough and Jones, *loc. cit.*). In all cases this enzyme preparation has catalysed the formation of ketoses with the D-*threo*-configuration at $C_{(3)}$ and $C_{(4)}$ (*i.e.*, D-*threo*pentulose derivatives) from a mixture of D-fructose 1 : 6-diphosphate and various aliphatic aldehydes, such as DL-lactaldehyde, glycolaldehyde, acetaldehyde, and aldotetroses. It was, however, found that L-glycerotetrulose was not formed by reaction with formaldehyde. On the other hand, Charalampous and Müeller (*J. Biol. Chem.*, 1953, **201**, 161; 1954, **211**, 249) have isolated from liver an enzyme preparation (1-phosphofructaldolase ?) which is not identical with muscle aldolase (1 : 6-diphosphofructaldolase ?), but which catalyses the reaction of formaldehyde and dihydroxyacetone

* Part VIII, *J.*, 1954, 3643.

phosphate to give L-*glycero*tetrulose 1-phosphate. Our failure to obtain L-*glycero*tetrulose may, however, be due to an inhibition of phosphatase activity by the formaldehyde present in the reaction mixture.

We have attributed the syntheses by the pea-enzyme preparation to the action of either a single aldolase or mixture of aldolases which causes reversible dismutation of D-fructose 1 : 6-diphosphate (I; P = PO_3Na_2) giving D-glyceraldehyde 3-phosphate (III) and dihydroxyacetone phosphate (II). In the presence of an introduced aldehyde, combin-



ation with dihydroxyacetone phosphate takes place to give a ketose 1-phosphate (IV). Although the phosphate esters have not been characterised in our products, we have assumed that hydrolysis of the ester takes place to give the free ketose (V), as a phosphatase has been shown to be present in the enzyme mixture.

It is significant that crystalline muscle aldolase (Byrne and Lardy, *Biochim. Biophys. Acta*, 1954, **14**, 495) and 1-phosphofructaldolase from liver (Leuthardt and Wolf, *Helv. Chim. Acta*, 1954, **37**, 1734) show the same specificity as the pea-enzyme preparation in giving ketose derivative with the D-*threo*-configuration at $C_{(3)}$ and $C_{(4)}$ from triose phosphate and aldehydes.

No evidence has been found to show that aldolase synthesises ketoses other than those having the D-*threo*-configuration at $C_{(3)}$ and $C_{(4)}$. However, D-tagatose 1 : 6-diphosphate, which has the L-*erythro*-configuration at $C_{(3)}$ and $C_{(4)}$, can be split by muscle aldolase between $C_{(3)}$ and $C_{(4)}$ (Tung, Ling, Byrne, and Lardy, *Biochim. Biophys. Acta*, 1954, **14**, 488).

Experimental

Evaporations were carried out under reduced pressure.

Condensation of Propionaldehyde with Triose Phosphate.—To disodium D-fructose 1 : 6-diphosphate (8 g.) in water (50 c.c.), freshly distilled propionaldehyde (5 c.c.) in water (100 c.c.) was added, and the resulting solution mixed with the enzyme preparation from pea seeds (100 g.) (Stumpf, *loc. cit.*; Hough and Jones, 1952, *loc. cit.*). The reaction mixture (pH 6) was incubated for 24 hr. at 22° and then adjusted to pH 5 by the addition of acetic acid. After 1 hr. at 90° to inactivate the enzymes, the solution was centrifuged to remove precipitated protein and the resulting supernatant liquor evaporated to dryness. Extraction of the residue with boiling acetone (500 c.c.), followed by evaporation of the extract, gave a golden syrup (1·07 g.). Examination on paper chromatograms (solvent: butan-1-ol–ethanol–water, 40 : 11 : 19 v/v) showed the presence of a sugar which was co-chromatographed with 5 : 6-dideoxy*threo*hexulose (rate of movement compared with rhamnose, 2·3; Gorin, Hough, and Jones, 1955, *loc. cit.*) and which gave a yellow colour with the *p*-anisidine hydrochloride and a pink colour with the diphenylamine–trichloroacetic acid spray reagents. Dihydroxyacetone was detected on the paper chromatogram by its brick-red colour with the *p*-anisidine hydrochloride reagent. It is probably an artefact from the breakdown of D-fructose 1 : 6-diphosphate.

The syrupy mixture was separated by chromatography on sheets of Whatman No. 1 filter paper (solvent: as above) and the appropriate sections of the paper chromatograms were cut out and eluted with water. After evaporation of the solvent, the fraction containing 5 : 6-dideoxy-D-*threo*hexulose (136 mg.) had $[\alpha]_D^{20}$ −13° (*c*, 1·2 in MeOH). Gorin, Hough, and Jones (1955, *loc. cit.*) quote $[\alpha]_D^{20}$ −8° (*c*, 2·5 in MeOH) for 5 : 6-dideoxy-D-*threo*hexulose, but this latter material may have been contaminated with a little 5 : 6-dideoxy-L-*erythro*hexulose. A portion of the hexulose was treated for 18 hr. with aqueous sodium hypoiodite at pH 11·4 under conditions specified by Chanda, Hirst, Jones, and Percival, (*loc. cit.*). It consumed

0·35 mol. of reagent per mol. of dideoxyhexulose, as compared with 0·94 mol. consumption when D-xylose was oxidised under the same conditions.

5 : 6-*Dideoxy*-D-threo*hexose Phenylosazone from* 5 : 6-*Dideoxy*-D-threo*hexulose*.—The dideoxyhexulose (91 mg.) in water was warmed at 40° for 16 hr. with 6 mol. of phenylhydrazine (0·40 c.c.) in acetic acid (0·6 c.c.). The precipitated phenylosazone was collected and washed with water. Two recrystallisations from benzene gave light yellow crystals (85 mg.) which had m. p. 160—171°, undepressed on admixture with authentic 5 : 6-dideoxy-D-*threo*hexose phenylosazone (Found : N, 16·9. Calc. for $C_{18}H_{22}O_2N_4$: N, 17·2%). The product gave an *X*-ray powder photograph indistinguishable from that given by the authentic material, and it showed $[\alpha]_D^{20}$ +32° (2 min.) ⟶ +8° ±8° (18 hr.; constant value; *c*, 0·17, in C_5H_5N–EtOH, 3 : 2 v/v). The phenylosazone prepared from 5 : 6-dideoxy-D-*xylo*hexose had $[\alpha]_D^{20°}$ +47° (5 min.) ⟶ +20° ± 7° [24 hr.; constant value; *c*, 0·60 in the same solvent (Gorin, Hough and Jones, 1955, *loc. cit.*)].

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The Alkaline Hydrolysis of Substituted Ethyl Benzoates. The Additive Effects of Substituents.

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A kinetic study is reported of the alkaline hydrolysis of 34 substituted ethyl benzoates. Of these, twenty were disubstituted and one trisubstituted; the remainder were monosubstituted esters whose rate constants were required for an analysis of the cumulative effects of groups on reactivity.

It has been shown that the resultant effect of two substituents, in those esters where the possibility of group interaction is at a minimum, is very close to the sum of their separate effects. In the remainder, the additive relationship is less exact.

THE discovery of a number of organic reactions in which the influence of polar substituents on the rates of reactions may be accounted for almost solely by changes in the energy of activation—the entropy of activation remaining virtually unchanged—led to a number of investigations of the cumulative effects of substituents. Until recently, almost all systematic studies covering a wide range of substituents were restricted to the determination of the influence of single substituents. Only for the nuclear chlorination of aromatic ethers of the types *p*-$RO{\cdot}C_6H_4X$ and $RO{\cdot}C_6H_3X_2$, where some two hundred ethers have been examined, had a comprehensive study been made of the influence of two or more substituents. Here the important conclusions were reached, not only that differences in rate resulting from the presence of substituents could be accounted for satisfactorily by changes in the energy of activation, but also that the resultant effect of two substituents is very closely the algebraic sum of their individual effects (*J.*, 1928, 1006; 1935, 1831; 1942, 418, 676; 1954, 1775).

In 1949 further evidence for the additive effect of substituents was revealed. Stubbs and Hinshelwood (*J.*, 1949, S 71) found that in the benzoylation of anilines a polar substituent at a given position in the aniline alters the free energy of activation ($-RT \ln k$) by an amount which is characteristic of the substituent and is independent of the presence of a second substituent, while Shorter and Stubbs (*J.*, 1949, 1180) showed from an analysis of the available dissociation constants of a wide range of benzoic acids that the change in the free energy of ionisation ($-RT \ln K$) produced by two or more substituents is in many

instances nearly the sum of the effect of these groups when present separately; the most notable exceptions are certain 2 : 6- and 2 : 3-disubstituted acids.

About the same time, evidence of a similar additivity was found for the alkaline hydrolysis of some disubstituted ethyl benzoates (Brynmor Jones and Robinson, *Nature*, 1950, **165**, 453), and more recently for the bromination of aromatic ethers by hypobromous acid in aqueous acetic acid (Branch and Brynmor Jones, *Research*, 1952, **5**, No. 7; *J.*, 1954, 2317; 1955, 2921).

The earlier studies of the alkaline hydrolysis of ethyl benzoates (cf. Ingold and Nathan, *J.*, 1936, 222; Evans, Gordon, and Watson, *J.*, 1937, 1430; Tommila and Hinshelwood, *J.*, 1938, 1801; Tommila, *Ann. Acad. Sci. Fennicae*, Ser. No. *A.* 57, No. 133, 1941 *et seq.*) had established that for a wide range of monosubstituted esters *meta*- and *para*-substituents markedly affect the energy of activation without appreciably altering the entropy factor. On the other hand, *ortho*-substituents, with the single exception of fluorine, affect both the energy and the entropy term.

The present investigation extends these studies to include some twenty disubstituted esters. In view of the known effect of *ortho*-substituents on the entropy of activation, the esters selected had the two substituents in either the 3 : 4- or the 3 : 5-positions. For the present analysis of additive effects comparable values were required also of the effects of a number of individual groups. The rates for thirteen monosubstituted ethyl benzoates have therefore been determined. These are given in Table 3. Where the rates had been determined by earlier workers, good agreement was found with the values in the present study. This is clear from the data in Table 1 where the rates of the substituted and the unsubstituted ethyl benzoates found by various workers are expressed as ratios (k_s/k_u). In four of the five investigations the solvent was aqueous ethyl alcohol. The values in column 5 were obtained by Tommila with aqueous acetone as medium, and the differences between the ratios in columns 5 and 6 may arise from the fact that the group dipole moments are not the same in the two solvents.

TABLE 1. *Comparison of the rates of hydrolysis of substituted and unsubstituted ethyl benzoates (given as velocity ratios, k_s/k_u).* (For references see text.)

Substituent	Ingold & Nathan	Evans, Gordon, and Watson	Kindler	Tommila	This paper
4-OMe	0·208	—	0·214	—	0·219
4-Me	0·456	—	0·480	0·396	0·458
4-Cl	4·31	—	4·33	4·04	4·34
3-Me	—	0·697	0·706	0·502	0·708
3-Cl	—	7·68	7·41	6·29	7·62
3-NO_2	—	69·08	63·48	47·21	68·3
4-NH_2	0·0231	—	0·0233	0·030	0·0244
3-OMe	—	—	1·20	1·355	1·33
3-Br	—	—	8·06	6·17	8·10
4-OEt	—	—	0·22	0·207	0·199
4-OPr^i	—	—	0·212	—	0·194
3-Me, 4-Me	—	—	0·333	—	0·320
3-Cl, 4-Cl	—	—	—	17·47	24·1
3-Br, 5-Br	—	—	—	31·20	65·2
3-Me, 5-Me	—	—	—	0·338	0·498

The velocities of reaction of four typical esters were determined at 25° and 35°, and the energies of activation and the entropy factors evaluated. These are given in Table 2.

TABLE 2.

Ester	10^3k_{25}	10^3k_{35}	$\log_{10} PZ$	E (cal.)
Et benzoate	0·607	1·61	9·8	17,730
Et 3 : 5-dimethylbenzoate	0·302	0·825	9·9	18,330
Et 4-methoxy-3-nitrobenzoate	6·36	15·90	9·8	16,330
Et 3 : 5-dibromobenzoate	39·6	60·95 (at 30°)	9·8	15,300

Complete lists of rate constants and of energies of activation are summarised in Tables 2—5. To facilitate comparison of these results with those for the benzoylation of anilines, the data are arranged in a similar manner (cf. Stubbs and Hinshelwood, *loc. cit.*).

TABLE 3. *Velocity constants and activation energies (E′) for monosubstituted ethyl benzoates.*

Subst.	10^5k_{25}	E′ (cal.) *	Subst.	10^5k_{25}	E′ (cal.) *	Subst.	10^5k_{25}	E′ (cal.) *
(H)	0·607	17,730 †	*p*-Cl	2·64	16,860	*p*-OEt	0·121	18,690
p-Me	0·278	18,190	*m*-Cl	4·63	16,530	*p*-OPr^i	0·118	18,700
m-Me	0·430	17,930	*m*-NO_2	41·5	15,230	*p*-O·CH_2·CH:CH_2	0·144	18,580
p-OMe	0·133	18,630	*m*-Br	4·92	16,490	*p*-O·CH_2Ph	0·140	18,600
m-OMe	0·805	17,560	*p*-NH_2	0·00148	—			

* Calc. as $E' = 2{\cdot}303\boldsymbol{R}T[\log_{10}(PZ)_{\mathrm{R}} - \log_{10}k_{25}]$.
† Calc. from log k_{25} with non-exponential term equal to that for ethyl benzoate.

TABLE 4. *Increments in activation energy due to single substituents.*

Subst.	ΔE′	Subst.	ΔE′	Subst.	ΔE′	Subst.	ΔE′
(H)	0	*m*-OMe	−170	*m*-NO_2	−2500	*p*-OPr^i	+970
p-Me	+460	*p*-Cl	−870	*m*-Br	−1240	*p*-O·CH_2·CH:CH_2	+850
m-Me	+200	*m*-Cl	−1200	*p*-OEt	+960	*p*-O·CH_2Ph	+870
p-OMe	+900						

TABLE 5. *Disubstituted ethyl benzoates.*

Substituents	10^5k_{25}	E′	E′ (predicted)	ΔE′	ΔE′ (predicted)	[ΔE′ − ΔE′ (predicted)]
H	0·607	17,730	—	—	—	—
3-Me, 4-Me	0·194	18,410	18,390	+680	+660	+20
3-Me, 5-Me	0·302	18,140	18,130	+410	+400	+10
3-Cl, 4-Me	1·97	17,030	16,990	−700	−740	+40
3-NO_2, 4-Me	16·8	15,760	15,690	−1970	−2040	+70
3-OMe, 4-OMe	0·214	18,350	18,460	+620	+730	−110
3-Cl, 4-OMe	0·709	17,640	17,430	−90	−300	+210
3-Br, 4-OMe	0·728	17,620	17,390	−110	−340	+230
3-NO_2, 4-OMe	6·36	16,340	16,130	−1390	−1600	+210
3-OMe, 5-OMe	1·04	17,410	17,390	−320	−340	+20
3-Cl, 4-OEt	0·649	17,690	17,490	−40	−240	+200
3-Br, 4-OEt	0·663	17,680	17,450	−50	−280	+230
3-Cl, 4-OPr^i	0·701	17,650	17,500	−80	−230	+150
3-Br, 4-OPr^i	0·699	17,650	17,460	−80	−270	+190
3-NO_2, 4-OPr^i	5·05	16,480	16,200	−1250	−1530	+280
3-Cl, 4-O·CH_2·CH:CH_2	0·763	17,590	17,380	−140	−350	+210
3-Cl, 4-O·CH_2Ph	0·748	17,600	17,400	−120	−330	+210
3-Cl, 4-Cl	14·6	15,850	15,660	−1880	−2070	+190
3-Cl, 5-Cl	39·7	15,250	15,330	−2480	−2400	−80
3-Br, 5-Br	39·6	15,260	15,250	−2470	−2480	+10
3-Br, 5-Me	3·45	16,700	16,690	−1030	−1040	+10
3-OMe, 4-OMe, 5-OMe	0·927	17,480	18,290	−250	+560	−810

DISCUSSION

Constancy of the Entropy Factor.—The present data show that for three disubstituted ethyl benzoates with divergent rates of hydrolysis the value of the entropy factor is virtually the same as for ethyl benzoate. When values of $\log_{10} k_{25}$ are plotted against E the points fall on, or near to, a line of slope $-2{\cdot}303\boldsymbol{R}T$.

Cumulative Effect of Substituents.—The rates of hydrolysis of the substituted ethyl *p*-alkoxybenzoates, except those containing an *iso*propoxy-group, give velocity ratios, k_X^{OR}/k_X^{OMe}, which are constant to within 4%. These results (Table 6), which are directly

TABLE 6. *Relative rates of hydrolysis of* 3-X-*substituted* 4-*alkoxybenzoic esters. Values of* $100k_X^{OR}/k_X^{OMe}$.

Subst. X	R = Me	Et	Pr^i	CH_2Ph	CH_2·CH:CH_2
H	100	91	89	105	108
Cl	100	92	99	106	108
Br	100	92	96	—	—
NO_2	100	—	79	—	—

analogous to those for the nuclear chlorination of ethers, where the constancy of the entropy factor has been determined experimentally (*J.*, 1942, 418), show that in ester hydrolysis the alkoxy-groups and the polar substituent contribute almost additively to the energy of

activation. The overall differences in the rates of hydrolysis, however, are much smaller than for halogenation and, on this evidence alone, the constancy of the entropy factor for a wider range of esters cannot be regarded as established. In the 3-substituted 4-alkoxybenzoic esters only one of the two variable substituents, the 3-substituent, is directly attached to the benzene nucleus, for the R group functions by modifying the directive power of the OR group, and esters in which the two substituents are directly attached to the nucleus were therefore examined.

If the entropy factor is assumed to be constant, the change in the energy of activation produced by single substituents may be calculated by means of the relation $\Delta E' = -2{\cdot}303RT \log_{10} k_s/k_u$; and, if moreover substituent effects are additive, the observed increment in activation energy due to two substituents will be the sum of the increments due to each substituent alone, *i.e.*, $\Delta E'_{XY} = \Delta E'_X + \Delta E'_Y$. For instance, in ethyl 4-methyl-3-nitrobenzoate the individual group increments are $E'_{3\text{-}NO_2}$ −2500 cal. and $E'_{4\text{-}Me}$ + 460 cal. The predicted additive increment should, therefore, be −2040 cal. The observed value is −1970 cal. The difference of 70 cal. is well within the probable deviation (estimated at 100 cal.) which could occur without infringement of the additive relationship. Analysed in this way, the results for the 3-substituted 4-alkoxybenzoic esters show that the average difference between the observed and the calculated increments is of the order of 200 cal.

Of the remaining ten esters, eight give results in very close agreement with the predicted values. Of these, five have the substituents in the 3 : 5-positions, where group interaction would be at a minimum, and three are derivatives of ethyl *p*-toluate. The other two esters, ethyl 3 : 4-dichlorobenzoate and ethyl 3 : 4-dimethoxybenzoate, give differences between observed and calculated values of E' of +190 and −110 cal. respectively (cf. Table 5).

It is not possible to compare the present data closely with those for the benzoylation of disubstituted anilines since, unfortunately, there are only four cases where the nature and the position of the substituents are the same in the two series. The differences between the observed and the calculated energy increments for these are given in Table 7. In three

TABLE 7. *Divergences between observed and calculated increments in activation energy.*

Subst.	Benzoyln. of anilines	Hydrol. of esters
3 : 4-Me_2	+40	+20
3 : 5-Me_2	+40	+10
3 : 5-Br_2	+190	+10
3-Cl, 4-Me	+60	+40

of the four cases there is excellent agreement. The difference of 190 cal. found in the benzoylation of 3 : 5-dibromoaniline must arise from experimental error. For the only other amine of like orientation, 3 : 5-dimethylaniline, the divergence is 40 cal.

It is difficult to estimate with certainty the divergences which may be allowed between observed and predicted changes in energy while maintaining the concept of additivity. For the benzoylation, Stubbs and Hinshelwood estimate the permissible divergence to be about ±75 cal., and they conclude that " the resultant effect of two substituents is very closely the sum of their individual effects," although for eight of the 21 disubstituted anilines the differences between the observed and predicted values of $\Delta E'$ are in the range 100—240 cal.

The present study shows that while the resultant effect of two substituents on the rates of hydrolysis of a wide range of ethyl benzoates may not be strictly additive in all cases it approximates closely to the sum of the individual effects in many cases. When the two substituents are in the 3 : 5-positions, the combined effect is the algebraic sum of their separate effects.

EXPERIMENTAL

Kinetic Measurements.—The method of Evans, Gordon, and Watson (*loc. cit.*) was adopted, but a minor modification was made to ensure a more precise definition of zero time. The ester and alkali solutions were mixed at 25° in equimolecular proportions (M/20) and, within a few seconds of mixing, 10 ml. of the mixture were withdrawn and the hydroxyl-ion concentration

was determined. This value was used as the initial concentration (a) in equation, $k = x/[ta(a - x)]$, where x is the change in concentration of hydroxyl ion in time t. In all instances the reaction was bimolecular and strictly quantitative. The precision of the experimental method was satisfactory, but unfortunately the most divergent rate constants in the series of disubstituted esters covered only a 200-fold range. Typical results are given below, with the rate constants expressed as l. mole^{-1} sec.$^{-1}$.

Rate of alkaline hydrolysis of ethyl 4-methyl-3-nitrobenzoate in 84·6% aqueous ethyl alcohol at 25°.

t (min.)	$a - x$	10^3k	t (min.)	$a - x$	10^3k
0	(a = 0·939)	—	0	(a = 0·950)	—
4	0·789	16·87	4	0·798	16·70
8	0·678	17·07	8	0·688	16·70
15	0·546	17·03	15	0·562	16·57
25	0·432	16·66	25	0·430	16·97
40	0·328	16·49	40	0·320	17·67
60	0·248	16·49	60	0·248	16·55
90	0·177	16·97	90	0·179	16·80
120	0·142	16·60	120	0·135	17·25
		Mean 16·77			Mean 16·90

Mean of two determinations 16·8.

Purification of the Alcohol.—The reaction medium was aqueous ethyl alcohol (84·6% w/w) prepared by diluting purified alcohol with freshly boiled, distilled water. Absolute alcohol was purified first by being refluxed with quicklime for 2 hr., and then allowed to remain in contact with the quicklime for 24 hr. Anhydrous silver oxide was added, and the alcohol shaken at intervals during 24 hr. The dry alcohol was distilled in an all-glass apparatus, with rigorous precautions to exclude moisture. The diluted alcohol had d_4^{20} 0·8319, corresponding to 84·6% w/w alcohol.

Mono- and Di-substituted Benzoic Acids and Esters.—Some of the esters were purchased. Liquids were fractionated thrice under reduced pressure, considerable head and tail fractions being rejected at each distillation, and the middle fractions only used for subsequent distillation. The b. p.s of the purified esters were: ethyl benzoate, 97°/20 mm.; ethyl *p*-anisate, 139°/25 mm.; ethyl cinnamate, 139·5°/17 mm. Ethyl *p*-aminobenzoate, crystallised from absolute alcohol, had m. p. 92°. Other esters, prepared from acids which were commercially available and had been crystallised to constant m. p. from acetic acid, were treated similarly. The physical constants of these acids and of their esters, which, when solid, were crystallised from absolute alcohol, were as follows:

Substituted benzoic acids		Et esters
m-Cl,	m. p. 158°	b. p. 120°/25 mm.
m-Br,	,, 155	,, 129°/11 mm.
m-NO_2,	,, 142	m. p. 42°
p-Cl,	,, 235	b. p. 115°/15 mm.
3 : 4-Cl_2,	,, 202	m. p. 37°

The remaining acids and esters were prepared by standard methods. *m*-Toluic acid, m. p. 110°, was obtained from *m*-toluidine *via* the nitrile. Its ester had b. p. 85°/2 mm. The alkoxybenzoic acids were obtained from the appropriate hydroxy-acids (cf. *J.*, **1929**, 2660; **1935**, 1874).

Alkoxybenzoic acids		Et esters
m-OMe,	m. p. 106°	b. p. 134·5°/20 mm.
p-OEt,	,, 194	,, 127°/3 mm.
p-OPr^i,	,, 163	,, 119°/2 mm.
p-O·CH_2Ph,	—	,, m. p. 46°

The *p*-alkoxybenzoic acids were chlorinated and brominated, in glacial acetic acid at room temperature, by dichloramine-T or bromine. Nitration of these acids and of *p*-toluic acid was carried out in the same solvent at 70° with fuming nitric acid. 3-Chloro-4-methoxybenzoic acid, m. p. 214°, gave an ethyl ester, m. p. 76°; 3-bromo-, m. p. 218°, and 3-nitro-4-methoxybenzoic acid, m. p. 192°, gave esters melting at 74° and 101° respectively.

For the preparation of 3 : 5-dichloro-, m. p. 184°, and 3 : 5-dibromo-benzoic acid, m. p. 230°, anthranilic acid was halogenated in acetic acid, deamination of the purified products giving the

3 : 5-dihalogenobenozic acids in high yield. Ethyl 3 : 5-dichloro- and 3 : 5-dibromo-benzoate had m. p. 37° and 58° respectively after crystallisations from ethyl alcohol.

3-Chloro-4-methylbenzoic acid, m. p. 198° (ethyl ester, b. p. 135°/14 mm.), was prepared by the Sandmeyer reaction from the amino-acid obtained by the reduction of 4-methyl-3-nitrobenzoic acid.

Methylation of orcinol, and oxidation of the 3 : 5-dimethoxytoluene with permanganate, gave 3 : 5-dimethoxybenzoic acid, m. p. 182° (ethyl ester, m. p. 27°). 3 : 4-Dimethylbenzoic acid, m. p. 166° (ethyl ester, b. p. 120°/12 mm.), was synthesised from 3 : 4-dimethylaniline and the intermediate dimethylbenzonitrile; the isomeric 3 : 5-dimethyl acid, m. p. 165°, was prepared by oxidation of mesitylene with hot dilute nitric acid (its ethyl ester distilled at 120°/10 mm.).

The physical constants and the analyses of a number of other *acids* and *esters* are given below, X being halogen or nitrogen.

Disubstituted benzoic acids.

		Found (%)				Required (%)		
	M. p.	C	H	X	Formula	C	H	X
3-Chloro-4-ethoxy	208°	54·3	4·7	17·7	$C_9H_9O_3Cl$	53·9	4·5	17·7
3-Bromo-4-ethoxy	210	45·1	3·7	32·7	$C_9H_9O_3Br$	44·1	3·7	33·0
3-Chloro-4-*iso*propoxy	127	56·0	5·2	17·1	$C_{10}H_{11}O_3Cl$	56·0	5·2	16·6
3-Bromo-4-*iso*propoxy	129	46·9	4·5	30·5	$C_{10}H_{11}O_3Br$	46·3	4·3	30·9
3-Nitro-4-*iso*propoxy	158	53·2	4·9	6·0	$C_{10}H_{11}O_5N$	53·3	4·9	6·2

Ethyl esters.

		Found (%)				Required (%)		
	M. p.	C	H	X	Formula	C	H	X
3-Chloro-4-ethoxy	51°	58·4	5·9	15·8	$C_{11}H_{13}O_3Cl$	57·8	5·7	15·5
3-Bromo-4-ethoxy	59	48·4	4·7	29·3	$C_{11}H_{13}O_3Br$	48·4	4·8	29·3
3-Chloro-4-*iso*propoxy	48	59·2	6·1	14·9	$C_{12}H_{15}O_3Cl$	59·4	6·2	14·6
3-Bromo-4-*iso*propoxy	50	50·2	5·1	27·9	$C_{12}H_{15}O_3Br$	50·2	5·2	27·9
3-Nitro-4-*iso*propoxy	52	57·2	6·0	5·8	$C_{12}H_{15}O_5N$	56·9	5·9	5·5
4-Allyloxy-3-chloro	63	59·8	5·8	15·0	$C_{12}H_{12}O_3Cl$	59·9	6·1	14·8
4-Benzyloxy-3-chloro	66	65·7	5·2	12·3	$C_{16}H_{15}O_3Cl$	66·1	5·2	12·2
3-Bromo-5-methyl	27	48·9	4·5	32·8	$C_{10}H_{11}O_2Br$	49·3	4·5	32·9

3 : 4 : 5-Trimethoxybenzoic acid, m. p. 168° (cf. *Org. Synth.*, Coll. Vol. I, 1st edn., 537), gave an ethyl ester, m. p. 56°.

3-Bromo-5-methylbenzoic acid. Two routes to this acid were investigated : one from 4-bromo-2-methylacetanilide, the other, which gave a better overall yield, from 4-methyl-2-nitroaniline. The aniline was brominated in acetic acid to give 2-bromo-4-methyl-6-nitroaniline, m. p. 66°, in 96% yield; diazotisation and deamination gave 3-bromo-5-nitrotoluene, m. p. 82°; reduction with freshly etched iron powder and concentrated hydrochloric acid in 50% aqueous alcohol then gave 3-bromo-5-methylaniline as the hydrochloride in 100% yield. A suspension of this hydrochloride (15 g.) in a mixture of concentrated hydrochloric acid (15 ml.) and water (100 ml.) at 0° was diazotised (5 g. of sodium nitrite in 20 ml. of water) and then neutralised carefully with sodium carbonate; this solution was added slowly with vigorous stirring to an ice-cold solution of potassium cuprocyanide [from cuprous cyanide (8 g.) in a solution of potassium cyanide (18 g. in 60 ml. of water)] covered with a layer of benzene (100 ml.). The solution was stirred for 30 min. at 0—5°, then for 2 hr. at room temperature, and warmed to 55°. The preparation was completed by steam-distillation, and the *nitrile*, after two crystallisations from carbon tetrachloride, was obtained as pale yellow prisms, m. p. 62° (Found : C, 49·5; H, 2·9; N, 7·2; Br, 40·5. C_8H_6NBr requires C, 50·0; H, 2·9; N, 7·1; Br, 40·8%). Hydrolysis of the nitrile with 60% sulphuric acid (90 min.) gave a theoretical yield of 3-bromo-5-methylbenzoic acid, which crystallised from alcohol as colourless prisms, m. p. 177°. Ethyl 3-bromo-5-methylbenzoate was obtained from alcohol as small colourless prisms, m. p. 27°.

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*Mycoceranic Acid. Part II.**

By G. S. Marks and N. Polgar.

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(+)-4-Methylhexacosan-2-one and several straight-chain ketones have been synthesised for comparison with two ketones resulting from the stepwise degradations of mycoceranic acid (cf. Part I*). The latter is now provisionally regarded as 2(*D*) : 4(*D*) : 6(*D*)-trimethyloctacosanoic acid,† and some preliminary studies in the synthesis of this acid are reported.

The synthesis of 2 : 4 : 6(*D*)-trimethyloctacosanoic acid is described.

Mycoceranic acid, a lævorotatory acid isolated from the lipids of tubercle bacilli, has been shown, by a series of stepwise degradations, to have the structure (I) where *n* is probably 21 (Part I*). It remained, therefore, to confirm the length of the normal chain. The degradation products already described include the ketones (II) and (III), and the first aim of the present work was to identify these ketones by synthesis.

The ketone (II), containing an asymmetric carbon atom, resulted from the above degradative studies in amounts which were insufficient for determining its rotation. However, the configuration of the asymmetric carbon atom of this ketone may be fixed by reference to another degradation product of mycoceranic acid, namely, the 2-methyl-substituted lævorotatory acid (IV) (cf. Part I*) of which $C_{(2)}$ corresponds to $C_{(4)}$ of the ketone (II). The lævorotatory form of 2-methyl-substituted carboxylic acids has been sterically related to *D*-(+)-glyceric aldehyde † (Ställberg-Stenhagen and Stenhagen, *Arkiv Kemi, Min., Geol.*, 1947, **24**, *B*, No. 9). This relationship was based upon the correlation of (+)-methylsuccinic acid with (+)-malic acid, established by the method of "quasi-racemates" (Fredga, *ibid.*, 1942, **15**, *B*, No. 23), and recently confirmed by direct chemical correlation (Freudenberg and Hohmann, *Annalen*, 1953, **584**, 54). From these considerations, the above ketone (II) is assigned to the *D*-series.

(I) $CH_3{\cdot}[CH_2]_n{\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}CO_2H$ $\quad$ $CH_3{\cdot}[CH_2]_n{\cdot}CO{\cdot}CH_3$ (III)

(II) $CH_3{\cdot}[CH_2]_n{\cdot}CHMe{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ $\quad$ $CH_3{\cdot}[CH_2]_n{\cdot}CHMe{\cdot}CO_2H$ (IV)

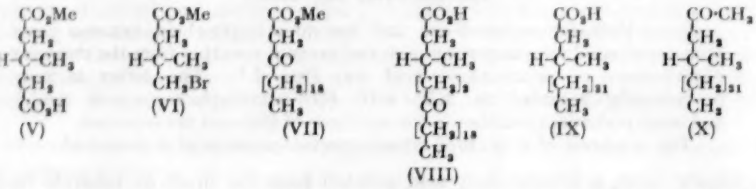
The *D*-form of 4-methylhexacosan-2-one (II; $n = 21$) was synthesised *via* *D*-3-methylpentacosanoic acid (IX). The starting point was *L*-(+)-methyl hydrogen 3-methylglutarate (V) (Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, 1947, **25**, *A*, No. 10; Linstead, Lunt, and Weedon, *J.*, 1950, 3333). This (and its enantiomorph) has been converted earlier into various long-chain 3-methyl-carboxylic acids by methods involving reaction of the half-ester chloride with a β-keto-ester (Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, 1948, **26**, *A*, No. 1; and later papers), or by the electrolysis of mixtures of the half ester and a fatty acid (Ställberg-Stenhagen, *Arkiv Kemi*, 1950, **2**, 95; Linstead, Lunt, and Weedon, *J.*, 1951, 1130). We found it advantageous to convert the half ester, by reaction of its silver salt with bromine (Hunsdiecker and Hunsdiecker, *Ber.*, 1942, **75**, 291) into (−)-(methyl *D*-4-bromo-3-methylbutanoate) (VI) (the change of prefix *L* to *D* is due to the conventional † alteration of the reference group), $[\alpha]_D$ −2·54°, which on refluxing with sodium iodide in acetone gave the corresponding iodo-ester. The latter, on reaction with the sodio-derivative of methyl 3-oxodocosanoate (VII) (obtained by the action of eicosanoyl chloride upon ethyl sodioacetoacetate), followed by hydrolysis and ketonic cleavage, afforded *D*-(+)-3-methyl-6-oxopentacosanoic acid (VIII), $[\alpha]_D$ +4·65°. This was converted by Clemmensen reduction into *D*-(+)-3-methylpentacosanoic acid (IX), $[\alpha]_D$ +3·76°, and thence, by reaction of the acid chloride with methylzinc iodide (Blaise, *Bull. Soc. chim. France*, 1911, **9**, pp. i—xxvi) into *D*-(+)-4-methylhexacosan-2-one (X), $[\alpha]_D$ +4·9°.

The semicarbazone of the ketone (X) had m. p. 101—102° which is some 9° higher than that reported (Part I, *loc. cit.*) for the semicarbazone of the degradation product (II) after only one crystallisation (owing to the small amounts of material available). The *X*-ray

* Part I, *J.*, 1954, 1011. The present paper is also regarded as "Constituents of the Lipids of Tubercle Bacilli. Part V." (Part IV, *J.*, 1954, 1011.)

† The symbols *D* and *L* are used in the sense defined by Linstead *et al.* (*J.*, 1950, 3333).

diffraction powder photographs, kindly taken by Mrs. D. M. Crowfoot Hodgkin, were very similar, but in the region of 20 Å the synthetic product gave a line, and the semicarbazone of the degradation product a rather broad region of heavy scattering, thus indicating the presence of a contaminant in the degradation product. For similar reasons an attempt



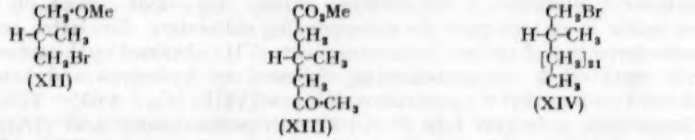
(V) (VI) (VII) (VIII) (IX) (X)

to identify the degradation product (III) (see above) by comparison of its semicarbazone with those of docosan-2-one, tricosan-2-one, and tetracosan-2-one (the preparations of these ketones are included in the Experimental section) has not so far been successful. A discussion on the question of the homogeneity of the lævorotatory acid employed for the degradative studies is reserved for a future communication. Meanwhile, mycoceranic acid is tentatively regarded as 2 : 4 : 6-trimethyloctacosanoic acid (I; $n = 21$).

In regard to the configurations of the asymmetric centres of mycoceranic acid it is of interest that mycoceranic acid, itself a 2-methyl-carboxylic acid, and also the 2-methyl-carboxylic acids (IV) (see above) and (XI) resulting from the stepwise degradations of mycoceranic acid (Part I, *loc. cit.*) are all lævorotatory. Although mycoceranic acid has additional asymmetric centres at $C_{(4)}$ and $C_{(6)}$ corresponding to $C_{(2)}$ of the acids (XI) and (IV), respectively, and the acid (XI) one additional centre of asymmetry at $C_{(4)}$, their rotatory powers, from comparison with optically active 2- and 4-methyl-carboxylic acids recorded in literature, appear to be largely due to the asymmetric centre at $C_{(2)}$. Since the lævorotatory form of 2-methyl-carboxylic acids has been assigned to the *D*-series (see above), it may be assumed that mycoceranic acid has *D*-configuration in respect of all three asymmetric centres.

(XI) $CH_3 \cdot [CH_2]_n \cdot CHMe \cdot CH_2 \cdot CHMe \cdot CO_2H$

In the course of investigations into the synthesis of 2(*D*) : 4(*D*) : 6(*D*)-trimethyl-octacosanoic acid we have devoted some attention to a route which involves the linking together, by a Grignard reaction, of two molecules each containing one optically active centre, *e.g.*, of (X) with (XII), or (XIII) with (XIV). Thus, condensation of the optically active ketone (X) with the Grignard derivative of the optically active bromide (XII), followed by dehydration of the resultant product, would give the ethylenic compounds (XV) which could be converted by catalytic hydrogenation into (XVI) with the newly created asymmetric centre at $C_{(4)}$. The latter, separated from each of the previously existing optically active centres at $C_{(2)}$ and $C_{(6)}$ by only one methylene group, may be expected to arise with a preponderance of one configuration, and it was of interest to study the direction and extent of this asymmetric synthesis. The isolation of the requisite diastereoisomer,



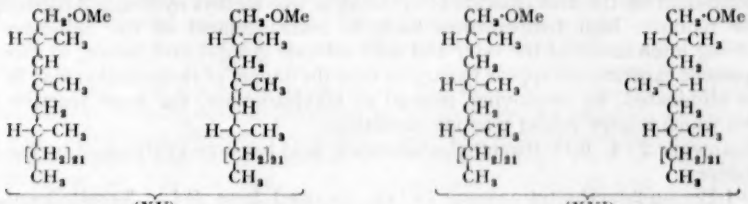
(XII) (XIII) (XIV)

if successful, would open the way to a synthesis of 2(*D*) : 4(*D*) : 6(*D*)-trimethyloctacosanoic acid by a further extension involving known procedures. Similar considerations apply to the modification of this scheme involving a Grignard reaction between (XIII) and (XIV).

The above approach is still under investigation, but some preliminary experiments in the synthesis of the requisite optically active intermediates are described below.

It was thought that the optically active methoxy-bromide (XII) might be accessible from the *L*-form of methyl 4-bromo-3-methylbutanoate (see above) by conversion into the

methoxy-ester (XVII), followed by hydrolysis, and reaction of the silver salt of the resulting acid with bromine. However, in a model experiment employing the *D*-form (VI) of methyl 4-bromo-3-methylbutanoate, reaction with sodium methoxide in methanol gave a product

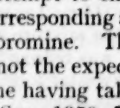


(XV) (XVI)

having $[\alpha]_D$ −85·4°, the analysis and high rotatory power of which indicated the structure of a *cyclo*propane derivative, arising by the elimination of hydrogen bromide.

In another experiment, reaction of the racemic form of methyl 4-bromo-3-methylbutanoate with silver carbonate in methanol (cf. Ziegler, Weber, and Gellert, *Ber.*, 1942, **75**, 1715) also failed to furnish the required methoxy-ester. An alternative procedure tried involved the conversion of the bromo-ester, by means of potassium acetate in glacial acetic acid, into the corresponding acetoxy-ester which was subjected to the action of methanolic hydrogen chloride to produce the hydroxy-ester. Methylation of the product by means of methyl iodide and silver oxide (Purdie and Irvine, *J.*, 1899, **75**, 485) failed, however, to yield the pure methoxy-ester, and owing to the unsatisfactory yields this approach was not pursued further.

In further experiments, methyl 3-methyl-4-phenoxybutanoate (XVIII) was obtained in 17% yield by reaction of phenol with methyl 4-iodo-3-methylbutanoate in the presence of potassium carbonate and methyl propyl ketone. Attempts to improve the yield of the phenoxy-ester by increasing the molar ratio of phenol to the iodo-ester failed, but the yield was slightly increased (to 21%) by using, as a solvent, acetone in place of methyl propyl ketone. In an attempt to employ this phenoxy-ester instead of the methoxy-derivative (see above), the corresponding acid was converted into its silver salt, and the latter subjected to the action of bromine. The product was, however, a bromo-acid of the composition $C_{11}H_{13}O_3Br$, and not the expected bromide (XIX), presumably substitution of the benzene nucleus by bromine having taken place. An analogous result is that of Dauben and Tills (*J. Amer. Chem. Soc.*, 1950, **72**, 3185) who obtained 2-bromo-5-methoxybenzoic acid on reaction of the silver salt of *m*-methoxybenzoic acid with bromine.



(XVII)

$MeO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}OPh$
(XVIII)

$Br{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}OPh$
(XIX)

Concurrently with the above studies, we also examined the preparation of the optically active keto-ester (XIII). The corresponding acid, obtained by Ställberg-Stenhagen (*Arkiv Kemi, Min., Geol.*, 1948, **26**, *A*, No. 12) by a procedure involving reaction of the acid chloride derived from the half ester (V) with the sodio-derivative of methyl aceto-acetate, was stated to show rotations varying considerably from one preparation to the other. This was explained by the existence of keto-acid–hydroxy-lactone tautomerism, and it was reported that a specimen of the keto-acid having α_D −3·3° (homog., *l*, 1) yielded on Clemmensen reduction (+)-3-methylhexanoic acid with $[M]_D$ +3·9°, to be compared with a previously recorded value of 3·6° (Levene and Marker, *J. Biol. Chem.*, 1932, **98**, 1). We tried to obtain the above keto-ester (XIII) in one stage by the action of methylzinc iodide on the acid chloride of the half ester (V). The product had $]\alpha]_D$ −1·1°, and gave on Clemmensen reduction, followed by hydrolysis, an acid having $[\alpha]_D$ +11·05°, $[M]_D$ +14·4°, values which are considerably higher than those quoted above for (+)-3-methylhexanoic acid. The presence, in small amounts, of an unsaturated contaminant arising from the

Clemmensen reduction is a possibility, and the product clearly requires further examination. It should be noted, however, that according to previous reports (Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, 1948, **26**, *A*, No. 12; Chase and Hey, *J.*, 1952, 553) the action of alkylcadmium on the acid chloride of optically active methyl hydrogen 3-methylglutarate at the requisite high temperatures leads to rearrangement of the half-ester chloride (involving interchange of the ester and acid chloride groups) and, hence, to racemisation. The present experiments appear to suggest that the danger of racemisation may be reduced, if not eliminated, by employing, instead of alkylcadmium, the more reactive alkylzinc halides which require milder reaction conditions.

Meanwhile 2 : 4 : 6(*D*)-trimethyloctacosanoic acid has been synthesised by the following procedure.

D-1-Bromo-2-methyltetracosane (XIV), obtained from *D*-(+)-3-methylpentacosanoic acid (IX) by reaction of its silver salt with bromine, gave by condensation with ethyl methylmalonate and the usual subsequent procedure 2 : 4(*D*)-dimethylhexacosanoic acid, characterised as its *p*-bromophenacyl ester, m. p. 67—73°. It is of interest that this melting point is close to the m. p. (68°) reported (Part I, *loc. cit.*) for the *p*-bromophenacyl ester of the degradation product (XI) mentioned earlier, now regarded as 2(*D*) : 4(*D*)-dimethylhexacosanoic acid. The above acid, by reduction with lithium aluminium hydride, followed by conversion of the resultant alcohol into the iodide, and condensation of the latter with ethyl methylmalonate, afforded 2 : 4 : 6(*D*)-trimethyloctacosanoic acid. This, representing a mixture of stereoisomers, differed in its m. p. (45°) and the m. p. of its *p*-bromophenacyl ester (62—67°) from those recorded (Chanley and Polgar, *J.*, 1954, 1003) for the naturally occurring acid and its derivative (30°, and 31·5° respectively), but the infrared spectra of the acids showed close agreement.

Experimental

Ketones.—Methyl iodide (5 g.) was added, according to the procedure of Blaise (*loc. cit.*), to a mixture of toluene (2·5 c.c.), ethyl acetate (1 g.), and zinc-copper couple (4·5 g.; prepared by Howard's method, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 677), and the mixture refluxed for 5 hr. It was then cooled with ice, and, after the addition of toluene (10 c.c.), the solution was decanted. A solution of the requisite acid chloride (about 1 g.) in toluene (15 c.c.) was introduced during 15 min. with cooling and stirring, and, after a further 5 min., the mixture was decomposed by pouring it on ice. The product, isolated in the known manner, was refluxed with 5% ethanolic potassium hydroxide (50 c.c.) for 0·5 hr. in order to hydrolyse any ester formed as a by-product. After acidification with dilute hydrochloric acid, the product was collected with ether, and the ethereal extract washed, successively, with aqueous potassium hydroxide and water, then dried ($MgSO_4$). Removal of the solvent gave the crude ketone.

The requisite acids were obtained from octadecan-1-ol, purified by distillation of its acetate through an 18-inch electrically heated column packed with wire-gauze rings, by standard homologation procedures. They were converted into the acid chlorides by means of thionyl chloride (purified by successive distillations from quinoline and linseed oil). The following ketones were obtained :

Docosan-2-one, after crystallisation from ethanol, had m. p. 64—65° (Found : C, 81·4; H, 13·5. $C_{22}H_{44}O$ requires C, 81·5; H, 13·6%). It gave a *semicarbazone*, m. p. 128—129° (from ethanol) (Found : C, 72·5; H, 12·2; N, 10·8. $C_{23}H_{47}ON_3$ requires C, 72·4; H, 12·3; N, 11·0%).

Tricosan-2-one, m. p. 66—67° (from ethanol) (Found : C, 81·9; H, 13·5. $C_{23}H_{46}O$ requires C, 81·7; H, 13·6%), gave a *semicarbazone*, m. p. 129·5—130·5° after crystallisation from ethanol (Found : C, 73·0; H, 12·4; N, 10·4. $C_{24}H_{49}ON_3$ requires C, 72·9; H, 12·4; N, 10·6%).

Tetracosan-2-one, m. p. 67—68° (from ethanol) (Found : C, 81·5; H, 13·4. $C_{24}H_{48}O$ requires C, 81·8; H, 13·6%), gave a *semicarbazone*, m. p. 131—131·5° (from ethanol) (Found : C, 73·1; H, 12·4; N, 10·0. $C_{25}H_{51}ON_3$ requires C, 73·4; H, 12·5; N, 10·3%).

(−)-(*Methyl* D-4-*bromo*-3-*methylbutanoate* (VI).—*L*-(+)-(Methyl hydrogen 3-methylglutarate) (V), α_D^{15} +0·72° (homog.; *l.* = 1), was obtained by Ställberg-Stenhagen's procedure (*Arkiv Kemi, Min., Geol.*, 1947, **25**, *A*, No. 10) with the modifications suggested by Linstead, Lunt, and Weedon (*loc. cit.*) [Ställberg-Stenhagen gives α_D^{22} +0·65° (homog.; *l* = 1); Linstead *et al.* give $\alpha_D^{17\cdot7}$ +0·65° (homog.; *l* = 1)]. An aqueous solution of the sodium salt, prepared by neutralising the half ester (20 g.) with N-sodium hydroxide (phenolphthalein), was added

dropwise with stirring to a warm solution of silver nitrate (21·3 g.) in water (90 c.c.), and the precipitated silver salt collected, washed, successively, with water, acetone, and ether, then dried *in vacuo* over calcium chloride, finely ground, and finally dried *in vacuo* over phosphoric oxide. A suspension of the silver salt (30 g.) in dry carbon tetrachloride (100 c.c.) was stirred and cooled with water while bromine (18 g.) was added slowly during 1 hr.; the mixture was then refluxed on the steam-bath for 1 hr., and, after cooling, filtered through glass-wool. The silver bromide remaining on the filter was washed with ether, and the ethereal washings were added to the filtrate. The solution was evaporated and the residue taken up in ether, then washed, successively, with 5% aqueous potassium hydroxide (to remove any acid), and water, and dried ($MgSO_4$). Distillation afforded (−)-(*methyl* D-4-*bromo*-3-*methylbutanoate*) (12·85 g.; 60%) as a slightly yellow liquid, b. p. 94—96°/20 mm., $[\alpha]_D^{17\cdot5}$ −2·54° (homog.; *l*, 0·5), n_D^{19} 1·4602 (Found: C, 37·65, 37·05; H, 5·9, 6·15; Br, 40·3. $C_6H_{11}O_2Br$ requires C, 36·95; H, 5·65; Br, 41·0%).

Methyl 3-*Oxodocosanoate* (VII) (cf. Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, 1945, **20**, *A*, No. 19).—(i) Benzene (250 c.c.) and ethyl acetoacetate (19·5 g.) were added to granulated sodium (3·3 g.), and the mixture was heated on a steam-bath with stirring for 3 hr. After the mixture had cooled to room temperature, eicosanoyl chloride (43·5 g.; obtained from eicosanoic acid, m. p. 75°, by means of thionyl chloride) in warm benzene was added dropwise, and the mixture refluxed with stirring for 15 min. The product was poured into dilute sulphuric acid, and, after the addition of ether, the organic layer separated, washed with water, and evaporated. The residue, dissolved in warm dry benzene (150 c.c.), was shaken with sodium methoxide in methanol (4·7 g. of sodium in 200 c.c. of methanol) for 20 hr. Acidification and ether-extraction, followed by removal of the solvents gave a product, m. p. 58—64° after successive crystallisations from ethanol and acetone (Found: C, 76·0; H, 12·4%). Titration of a 0·5-g. portion, dissolved in warm ethanol, with aqueous-ethanolic potassium hydroxide indicated the presence of about 30% of eicosanoic acid. The titrated solution deposited on cooling a mixture of potassium eicosanoate and methyl 3-oxodocosanoate. This was treated with hot light petroleum (b. p. 40—60°) in which the methyl ester was readily soluble and the potasium salt almost insoluble. Evaporation of the solution, followed by crystallisation of the residual product from ethanol, furnished methyl 3-oxodocosanoate, m. p. 62—62·5° (Found: C, 75·1; H, 11·9. Calc. for $C_{23}H_{44}O_3$: C, 75·0; H, 12·0%). Ställberg-Stenhagen (*loc. cit.*) records m. p. 62·6°.

(ii) The product resulting on reaction of eicosanoyl chloride (93 g.) with ethyl sodioacetoacetate (from 45·5 g. of ethyl acetoacetate, and 7·5 g. of sodium), as described above, was dissolved in warm benzene (380 c.c.) and kept with sodium (12 g.) in methanol (450 c.c.) for 20 hr. with occasional warming and shaking. The product was acidified with dilute hydrochloric acid, ether added, and the benzene–ether layer washed successively with water, 1% aqueous potassium hydroxide (to remove eicosanoic acid) (ethanol was added to break the resulting emulsion), and water, and dried ($MgSO_4$). Evaporation, followed by crystallisation of the residual product from ethanol, gave methyl 3-oxodocosanoate (30·5 g., 29%), m. p. 62—62·8° (Found: C, 75·0; H, 12·1%).

D-(+)-3-*Methyl*-6-*oxopentacosanoic Acid* (VIII).—Methyl *D*-4-iodo-3-methylbutanoate (9 g.; obtained from the corresponding bromo-derivative by refluxing it with sodium iodide in acetone) was refluxed with methyl 3-oxodocosanoate (13·6 g.) in methyl propyl ketone (152 c.c.), and dry potassium carbonate (30 g.) for 20 hr. (cf. Ställberg-Stenhagen and Stenhagen, *Arkiv Kemi, Min., Geol.*, 1944, **19**, *A*, No. 1). Water and ether were then added, the organic layer was washed with water and dried ($MgSO_4$), and the solvents were removed by distillation. The residue, taken up in warm benzene (44 c.c.), was kept with a solution of potassium hydroxide (34·6 g.) in water (34·6 c.c.) and methanol (520 c.c.) at 50° for 20 hr. The mixture was then acidified (dilute hydrochloric acid) and extracted with warm benzene, and the benzene extract was washed with warm water and evaporated. The residue, after successive crystallisations from acetone and light petroleum (b. p. 60—80°), gave D-(+)-3-*methyl*-6-*oxopentacosanoic acid* (7·5 g., 50%), m. p. 74·5—75·5°, $[\alpha]_D^{17}$ +4·65° (*c*, 7·95 in $CHCl_3$; *l*, 1) (Found: C, 75·6; H, 12·1. $C_{26}H_{50}O_3$ requires C, 76·1; H, 12·2%).

D-(+)-3-*Methylpentacosanoic Acid* (IX).—Amalgamated zinc (180 g.) was added to a solution of the above keto-acid (7·1 g.) in ethanol (180 c.c.), and a current of hydrogen chloride passed into the solution until saturation. After refluxing for several hours, the solution was again saturated with hydrogen chloride, and this process repeated 3 times with 4—6 hr. intervals. The viscous mixture was then cooled, water added, and the product collected with ether. After evaporation of the ethereal solution, the residue was subjected to a repetition of the above reduction procedure. Hydrolysis of the reduced ester with ethanolic potassium hydroxide, followed by crystallisation of the resulting crude acid from light petroleum (b. p. 60—80°),

afforded D-(+)-3-*methylpentacosanoic acid* (5·65 g., 83%), m. p. 67—68·5°, $[\alpha]_D^{17}$ +3·76° (*c*, 4·52 in $CHCl_3$; *l*, 1) (Found : C, 78·5; H, 13·0. $C_{26}H_{52}O_2$ requires C, 78·8; H, 13·1%).

D-(+)-4-*Methylhexacosan*-2-*one* (X).—The preceding acid (1·8 g.) was converted, by means of thionyl chloride, into the acid chloride which, by reaction with methylzinc iodide in the manner already described afforded D-(+)-4-*methylhexacosan*-2-*one* (0·7 g.), m. p. 52·5—53·5° (from ethanol), $[\alpha]_D^{22}$ +4·9° (*c*, 6·31 in $CHCl_3$; *l*, 1) (Found : C, 81·7; H, 13·5. $C_{27}H_{54}O$ requires C, 82·2; H, 13·7%). Its *semicarbazone* had m. p. 101—102° after crystallisation from ethanol (Found : C, 74·4; H, 12·3; N, 9·2. $C_{28}H_{57}ON_3$ requires C, 74·5; H, 12·6; N, 9·3%).

Reaction of (−)-(*Methyl* D-4-*Bromo*-3-*methylbutanoate*) *with Sodium Methoxide*.—The bromo-ester (12 g.) was refluxed with methanolic sodium methoxide (35 c.c.; equiv. to 1·8 g. of sodium) for 4 hr. The solution was concentrated to a smaller volume, acidified (dilute hydrochloric acid), and extracted with ether. Distillation furnished a colourless liquid (3·8 g.), b. p. 62°/85 mm., $[\alpha]_D^{17}$ −85·4° (*c*, 13·09 in Et_2O; *l*, 1). The analytical results (Found : C, 62·8, 62·9; H, 8·8, 8·6. Calc. for $C_6H_{10}O_2$: C, 63·15; H, 8·8%) suggest that elimination of hydrogen bromide has occurred, giving rise to a *cyclo*propane derivative.

Attempted Preparation of Methyl 4-*Methoxy*-3-*methylbutanoate*.—(i) Methyl 4-iodo-3-methylbutanoate (5·3 g.; obtained by the procedure already described for the optically active ester) was refluxed with methanol (20 c.c.) in the presence of silver carbonate (13·7 g.) for 11 hr. Ether was then added, and the solution filtered, and, after being washed with water, dried ($MgSO_4$). Distillation afforded the fractions, (a) b. p. 80—86° (Found : C, 55·0; H, 7·9. Calc. for $C_7H_{14}O_3$: C, 57·5; H, 9·6%), and (b) b. p. 140° (Found : C, 58·6; H, 9·6%).

(ii) Methyl 4-bromo-3-methylbutanoate (31·4 g.; prepared as shown for the optically active form) was added to a solution of potassium acetate in glacial acetic acid (obtained by heating gently 55 g. of dry potassium acetate in 220 c.c. of glacial acetic acid until 110 c.c. of the latter had distilled), and the solution refluxed with stirring for 12 hr. Dilution with water, and ether-extraction furnished *methyl* 4-*acetoxy*-3-*methylbutanoate* (16 g., 58%) as a colourless liquid, b. p. 112—113°/20 mm., n_D^{18} 1·4266 (Found : C, 54·95; H, 8·0. $C_8H_{14}O_4$ requires C, 55·2; H, 8·1%). This was dissolved in dry methanol (100 c.c) containing 2·5% of hydrogen chloride, and the solution distilled slowly from a flask fitted with a fractionating column at such a rate that after 20 hr. approximately two-thirds of the solvent had distilled. Evaporation of the remaining solution under reduced pressure, followed by refluxing the residue with methyl iodide (170 g.), anhydrous calcium sulphate (20 g.), and silver oxide (35 g.; added in 4 portions) for 24 hr., gave on addition of ether and distillation of the filtered solution a colourless liquid, b. p. 84—90°/18 mm. (Found : C, 58·8; H, 8·1%).

Methyl 3-*Methyl*-4-*phenoxybutanoate* (XVIII).—(i) Potassium carbonate (29 g.) was added to a solution of phenol (3·4 g.) and methyl 4-iodo-3-methylbutanoate (8·7 g.) in methyl propyl ketone (140 c.c.), and the mixture refluxed for 14 hr. Ether was then added, and, after filtration, the ethereal solution washed successively with water, aqueous potassium hydroxide, and water, then dried ($MgSO_4$), and distilled, affording *methyl* 3-*methyl*-4-*phenoxybutanoate* (1·3 g., 17%) as a colourless oil, b. p. 146°/16 mm. (Found: C, 68·9; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

On employing acetone as the solvent instead of methyl propyl ketone the yield was increased to 21%.

(ii) A mixture of powdered sodium (0·8 g.), phenol (6·6 g.), and toluene (20 c.c.) was heated under reflux, with stirring, until all the sodium had reacted. Methyl 4-iodo-3-methylbutanoate (6 g.) was then added, and the mixture refluxed for 1 hr. After dilution with water, and ether-extraction, the ethereal solution was washed with 5% aqueous potassium hydroxide, and water, and dried ($MgSO_4$). Distillation afforded only a few drops of a colourless oil, b. p. 133°/7 mm., presumably the desired phenoxy-ester.

3-*Methyl*-4-*phenoxybutanoic Acid*.—Hydrolysis of the preceding ester with 20% aqueous potassium hydroxide gave the *acid* as a viscous liquid, b. p. 180°/20 mm. (Found : C, 67·5; 67·4; H, 6·8, 7·2. $C_{11}H_{14}O_3$ requires C, 68·1; H, 7·2%).

Attempted Preparation of 1-*Bromo*-2-*methyl*-3-*phenoxypropane* (XIX).—The above phenoxy-acid (2·3 g.) was converted into the ammonium salt by the addition of a slight excess of concentrated aqueous ammonia. Water (27 c.c.) was then added, the solution boiled for a short time to remove the excess of ammonia, and silver nitrate (2·3 g.) in water (10 c.c.) added. The precipitated silver salt was washed, dried, and caused to react with bromine (2 g.) in the presence of carbon tetrachloride (15 c.c.) as described for a previous case. The ethereal extract of the product, after being washed with 5% aqueous potassium hydroxide, yielded on evaporation practically no residue. The alkaline washings on acidification, followed by ether-extraction, and distillation, afforded a product (2·45 g.), b. p. 187°/0·1 mm., which after crystallisation

from light petroleum (b. p. 40—60°) had m. p. 79·5—80°, and appeared to be a bromo-derivative of 3-methyl-4-phenoxybutanoic acid (Found : C, 48·1; H, 4·8; Br, 29·0. Calc. for $C_{11}H_{13}O_3Br$: C, 48·4; H, 4·8; Br, 29·3%).

(−)-*Methyl* 3-*Methyl*-5-*oxohexanoate* (XIII).—Oxalyl chloride (6·4 g.) was added to *L*-(+)-methyl hydrogen 3-methylglutarate (6 g.) in benzene (30 c.c.), and the solution kept at 30° for 3 hr. The solvent and excess of oxalyl chloride were removed under reduced pressure at 40° (bath); more benzene was added, and the process repeated. The resulting acid chloride was then dissolved in toluene (8 c.c.), and caused to react with a solution of methylzinc iodide (from 16·2 g. of methyl iodide, 8 c.c. of toluene, 3·3 g. of ethyl acetate, and 14·7 g. of zinc-copper couple) in the manner already described. Distillation afforded a product, b. p. 98—100°/13 mm., which on redistillation yielded (−)-*methyl* 3-*methyl*-5-*oxohexanoate* as a colourless oil (3·8 g., 65%), b. p. 99°/13 mm., $[\alpha]_D^{16}$ −1·1° (*c*, 35·60 in Et_2O; *l*, 0·5), n_D^{17} 1·4290 (Found : C, 60·3; H, 8·7. $C_8H_{14}O_3$ requires C, 60·75; H, 8·9%).

A 1·8-g. portion of this keto-ester gave on Clemmensen reduction as described for a previous example, followed by hydrolysis of the reduced ester with 15% aqueous potassium hydroxide, (+)-3-methylhexanoic acid as a colourless oil (0·5 g.), b. p. 170° (bath)/80 mm., $[\alpha]_D^{18}$ +11·05° (*c*, 6·69 in C_6H_6; *l*, 0·5), $[M]_D^{18}$ +14·4°, n_D^{18} 1·4308 (Found : C, 65·0; H, 10·5. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·8%). Levene and Marker (*J. Biol. Chem.*, 1931, **91**, 77) record $[\alpha]_D^{20}$ −3·1° (in C_6H_6), n_D^{25} 1·4214, for the (−)-form.

D-1-*Bromo*-2-*methyltetracosane* (XIV).—Reaction of the silver salt of *D*-(+)-3-methylpentacosanoic acid (4·72 g.; obtained by precipitation of an ethanolic solution of the potassium salt with ethanolic silver nitrate, followed by washing of the precipitate, successively, with warm water, ethanol, and ether, and drying over phosphoric oxide in a desiccator, then *in vacuo* at 100°) with bromine (1·5 g.) in carbon tetrachloride (30 c.c.) by the procedure previously described gave D-1-*bromo*-2-*methyltetracosane* (1·3 g.), m. p. 40—41° after crystallisation from acetone (Found : Br, 19·25. $C_{25}H_{51}Br$ requires Br, 18·55%).

2 : 4(D)-*Dimethylhexacosanoic Acid*.—The above bromide (2 g.) was added to the sodio-derivative of ethyl methylmalonate, prepared from sodium (0·22 g.), ethanol (6 c.c.), and ethyl methylmalonate (3·3 g.), and the mixture refluxed for 10 hr. After acidification with dilute hydrochloric acid, the resulting alkylated malonic ester was collected with the aid of ether. Hydrolysis and decarboxylation in the usual manner gave a product which distilled at 190° (bath)/0·01 mm., and, after crystallisation from light petroleum (b. p. 40—60°), afforded 2 : 4(D)-*dimethylhexacosanoic acid* (0·8 g.), m. p. 54—55° (Found : C, 79·2; H, 13·1. $C_{28}H_{56}O_2$ requires C, 79·2; H, 13·2%), showing no measurable rotation (*c*, 7·65 in $CHCl_3$; *l*, 1). Its p-*bromophenacyl ester* had m. p. 67—73° (from ethanol) (Found : C, 69·6; H, 9·8. $C_{36}H_{61}O_3Br$ requires C, 69·6; H, 9·8%).

2 : 4(D)-*Dimethylhexacosan*-1-*ol*.—The preceding acid (1 g.) in ether (8 c.c.) was added to a solution of lithium aluminium hydride (0·3 g.) in ether (10 c.c.), and the mixture refluxed, with stirring, for 3 hr. Next day the excess of lithium aluminium hydride was decomposed by the addition of ethyl acetate; water was then added, followed by the addition of dilute sulphuric acid. After removal of the ethereal layer, the aqueous phase was extracted with ether, and the combined ethereal solutions were washed with 5% aqueous potassium hydroxide, water, and dried ($MgSO_4$). Distillation afforded 2 : 4(D)-*dimethylhexacosan*-1-*ol* (0·82 g.), b. p. 215° (bath)/0·01 mm., m. p. 52—55° (Found : C, 81·6; H, 13·9. $C_{28}H_{58}O$ requires C, 81·9; C, 14·1%).

2 : 4 : 6(D)-*Trimethyloctacosanoic Acid*.—The above alcohol was converted into the iodide by heating it (0·73 g.) with red phosphorus (0·03 g.) and iodine (0·35 g.) at 180° (bath) for 3 hr. The iodide, b. p. 210—225°(bath)/0·01 mm., isolated in the known manner, on condensation with the sodio-derivative of ethyl methylmalonate (from 0·083 g. of sodium, 2 c.c. of ethanol, and 1·25 g. of ethyl methylmalonate), followed by the usual successive stages (hydrolysis, decarboxylation), gave a product which distilled at 220—240°(bath)/0·01 mm., and, after crystallisation from light petroleum (b. p. 40—60°) at 0°, afforded the required *acid*, m. p. 45° (Found : C, 80·2; H, 13·2. $C_{31}H_{62}O_2$ requires C, 79·8; H, 13·3%); the p-*bromophenacyl ester* had m. p. 62—67° (from ethanol) (Found : C, 70·9; H, 10·2; Br, 11·9. $C_{39}H_{67}O_3Br$ requires C, 70·6; H, 10·1; Br, 12·05%).

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The Reaction of Binuclear Halogen-bridged Complexes of Platinum(II) with Monoamines.

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The reactions of a number of amines (am) with bridged compounds $L_2Pt_2X_4$ are described:

$$L_2Pt_2X_4 + 2am \rightleftharpoons 2[L,amPtX_2]$$

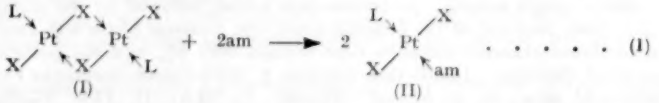
The uncharged ligands, L, are of the types C_2H_4, amines, PR_3, $P(OR)_3$, AsR_3, SbR_3, R_2S, R_2Se, and R_2Te, and the halogen, X, is usually chlorine.

When X is chlorine or bromine the equilibrium lies well to the side of the "mixed" product, unless the amine is very weakly basic, or sterically hindered. In the iodide series the equilibrium lies more to the left-hand side and the crystalline mixed complex can be difficult to isolate because $L_2Pt_2X_4$ is usually the least soluble component.

Generally the reaction proceeds rapidly to give "mixed" complexes of *trans*-configuration except when L is an amine. The reaction is then very slow, and the product a mixture of *cis*- and *trans*-isomers unless the amine is strongly hindered (the *trans*-isomer may then be the only product). The directing effects of the ligands, L, are most strongly marked in the reactions: (*a*) of ethylene with the amine bridged complex, $am_2Pt_2Cl_4$, which gives exclusively *cis*-$[C_2H_4,amPtCl_2]$, and (*b*) of an amine with the ethylene-bridged complex, $(C_2H_4)_2Pt_2Cl_4$, which gives only the *trans*-isomer.

The chloro-complexes *trans*-$[L,amPtCl_2]$ have moderate to high stabilities except when L is C_2H_4, SbR_3, R_2Se, or R_2Te; then dissociation and disproportionation occur easily.

A SERIES of complex compounds of the type *trans*-$[L,amPtCl_2]$ (II) (L = a wide variety of uncharged ligands, am = ammonia or a monoamine, and X = a halogen) was required for the study of inductive and mesomeric effects in complex compounds of platinum(II). The reaction of binuclear halogen-bridged complexes (Chatt and Venanzi, *J.*, 1955, 2787) with amines was therefore investigated as a general preparative method. This "bridge-splitting" reaction may generally be represented as follows although the product does not necessarily have a *trans*-configuration.



(I) (II) . . . . . (I)

The ligands, L, were chosen to have as great a variety of donor atoms as possible and were of the types: C_2H_4, amines, PR_3, $P(OR)_3$, AsR_3, SbR_3, R_2S, R_2Se, and R_2Te. Since we desired products soluble in carbon tetrachloride the sizes of the alkyl groups (R) were so chosen as to give this solubility.

The addition of ammonia and amines to compounds of the empirical formula, $LPtCl_2$ (now known to be dimeric), is one of the earliest known properties of such compounds. However, an excess of ammonia or amine was usually employed and the products were often more complex than indicated by reaction 1. Nevertheless a simple compound, now known to be *cis*-$[P(OEt)_3,p$-toluidine$PtCl_2]$, was isolated (Schützenberger and Fontaine, *Bull. Soc. chim. France*, 1872, **18**, 101). Rosenheim and Levy (*Z. anorg. Chem.*, 1905, **43**, 34) later prepared both the white *cis*- and the yellow *trans*-$[P(OEt)_3,PhNH_2PtCl_2]$ by treating $\{P(OEt)_3\}_2Pt_2Cl_4$ with aniline in hot and cold ethanolic solution respectively. The configurations were assigned by Troitskaya (*Zhur. priklad. Khim.*, 1953, **26**, 781). Of the bridged complexes of the sixth-group alkyls, Petren (Diss., Lund, 1898, p. 40) reported

that Svensson obtained [Et_2S,pyridine$PtCl_2$] from $(Et_2S)_2Pt_2Cl_4$ and pyridine, but in the selenide series only disproportionation occurred leading to $(Et_2Se)_2PtCl_2$ and $(pyridine)_2PtCl_2$. Klason (*Ber.*, **1904**, **37**, **1349**) also prepared this substance, now known to be *trans*-[Et_2S,pyridine$PtCl_2$], which he noted is converted into its *cis*-isomer on melting.

More recently it was shown by Mann and his co-workers (*Ann. Reports*, **1938**, **35**, **148**; Chatt and Mann, *J.*, **1939**, **1622**) that similar bridge-splitting reactions occur in the analogous series of palladium(II) bridged complexes and by Chatt (*J.*, **1951**, **652**) for the bridged series $(MPr^n_3)_2Pt_2Cl_4$ (M = P, As, and Sb).

The investigation to be described is concerned mainly with the reactions of a variety of amines with chloro-bridged complexes, $L_2Pt_2Cl_4$, having as great a diversity of donor atoms in the ligands, L, as possible. Generally the reaction proceeds very satisfactorily at room temperature with the reactants in acetone solution or with the bridged complex in acetone suspension. The yield of crude *trans*-[L,am$PtCl_2$] is often almost quantitative. However, considerable loss of product usually occurs during the purification by recrystallisation because the compounds *trans*-[L,am$PtCl_2$] which we prepared tend to have inconveniently high solubilities in organic solvents.

In carrying out the bridge-splitting reaction it is preferable to use the stoicheiometric quantity of amine because an excess facilitates the formation of by-products.

In general, the bridge-splitting reaction appears to be reversible but at the normal concentrations of reactants used in preparative work the equilibrium lies well to the side of the mixed complex, *trans*-[L,am$PtCl_2$]. This is certainly true of the splitting of $(PPr^n_3)_2Pt_2Cl_4$ by *p*-toluidine (Chatt and Hart, *J.*, 1953, 2363). However, when a weakly basic or sterically hindered amine is used to split the bridge the position of equilbrium lies so far in favour of the bridged complex as to cause difficulty in isolating the mixed complex.

Thus no diphenylamine complex could be isolated from the reaction of that amine with $(PPr^n_3)_2Pt_2Cl_4$ although the equilibrium (2) contains an appreciable proportion of the diphenylamine complex.

$$(PPr^n_3)_2Pt_2Cl_4 + 2Ph_2NH \rightleftharpoons 2trans\text{-}[PPr^n_3,Ph_2NHPtCl_2] \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In general, in these circumstances, only the original bridged complex can be isolated because it is the least soluble component of the mixture; the equilibrium must lie well to the right-hand side to allow the isolation of the mixed complex.

Factors Dependent on the Halide Bridge.—The effect of different halogens in the bridged system was investigated only in the series $(PPr^n_3)_2Pt_2X_4$ (X = Cl, Br and I). The equilibrium appears to lie increasingly in favour of the bridged complex as chlorine is replaced by bromine, and bromine by iodine. The bromides $(PPr^n_3)_2Pt_2Br_4$ and $(Bu^n_2S)_2Pt_2Br_4$ were both split and the products isolated as with the chlorides. However, the stability of the iodo-bridged system is so far in favour of the bridged complex that it is sometimes difficult to isolate the crystalline product, *trans*-[PPr^n_3,amPtI_2]. Even when *trans*-[L,amPtI_2] is prepared directly (from the corresponding chloride and potassium iodide in acetone solution) it is so labile that it tends to lose amine and form the bridged iodide before it can be isolated. The preparation of *trans*-[L,amPtI_2] where " am " is a volatile amine, *e.g.*, ammonia, is therefore especially difficult.

Factors Dependent on the Ligand L.—Only the chloro-bridged complexes were investigated in detail. The ligand, L, determines to some extent the configuration of the product. In the substitution reactions of complex ions of platinum(II) in aqueous solution, some ligands already present in the complex ion tend to direct incoming groups into the *cis*-positions to themselves. Others direct them into the *trans*-positions (see Quagliano and Schubert, *Chem. Rev.*, **1952**, **50**, **201**). *cis*-Substitution is slow and *trans*-substitution is rapid, somewhat analogous to *meta*- and *ortho-para*-substitution in benzene chemistry. Of the ligands, L, examined in this study, amines are known to be most strongly *cis*-directing and ethylene most strongly *trans*-directing. The relative strengths of the *trans*-directing effects of the remainder are not known with any certainty (see Chatt and Williams, *J.*, 1951, 3061; Hel'man and Karandashova, *Doklady Akad. Nauk S.S.S.R.*, **1952**, **87**,597).

All the bridged complexes, except those of the amines, react rapidly to give only the *trans*-isomer in the bridge-splitting reaction, although isomerisation may sometimes occur

subsequently. The contrast between the rates at which the olefin and amine chloro-bridged complexes were split is, however, very marked. Amines react almost instantaneously with a solution of $(C_2H_4)_2Pt_2Cl_4$ at $-70°$ and in the one example which has been investigated (with 4-*n*-pentylpyridine) the immediate product had a *trans*-configuration (Chatt and Venanzi, *loc. cit.*). On the other hand amines, am, react extremely slowly with solutions of the amine-bridged complexes, $am'_2Pt_2Cl_4$. With stoicheiometric proportions at room temperature the reaction was not complete after a week and so it was carried out at the boiling point of acetone ($\frac{1}{2}$ hr.) with an excess of the amine. Under both of these conditions the product was a mixture of *cis*- and *trans*-[am',amPtCl$_2$], although we cannot be certain whether both isomers were produced directly in the reaction, or whether one was formed from the other by subsequent isomerisation. However, the directing effects of amines and olefins are strikingly illustrated by the two bridge-splitting reactions (3) and (4) in dichloromethane and ethanol respectively; each leads to only one of the two possible isomeric products.

$$(pip)_2Pt_2Cl_4 + 2C_2H_4 \xrightarrow{15°} cis\text{-}[C_2H_4,pipPtCl_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$(C_2H_4)_2Pt_2Cl_4 + 2pepy \xrightarrow{-70°} trans\text{-}[C_2H_4,pepyPtCl_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

(pip = piperidine; pepy = 4-*n*-pentylpyridine)

The nature of the ligands, L, also has considerable effect on the stabilities of the mixed complexes, as is discussed below.

Factors Dependent on the Amine.—In general the amines used showed very similar behaviour when the chloro-bridged systems were split. The only marked differences were that sterically hindered amines, *e.g.*, 2 : 6-dimethylaniline, gave only the *trans*-isomer on fission of the amine-bridged complexes, $am_2Pt_2Cl_4$, and it was not always possible to isolate the product when weakly basic amines were used to split the bridge, as discussed above.

The splitting of amine-bridged complexes, possibly because of the more drastic conditions necessary for a reasonable rate of reaction, does not always give well-defined products, this depending to some extent on the amine used to split the bridge. Thus (4-*n*-pentylpyridine)$_2Pt_2Cl_4$ with 4-*n*-dodecylaniline gives only brown tars, yet with 2 : 6-dimethylaniline and 2 : 6-dibromo-4-*n*-dodecylaniline the bridge-splitting reactions were normal.

Properties of the Complexes of the Type trans-[L,amPtCl$_2$].—The new compounds of *trans*-configuration prepared by the bridge-splitting reaction (1) are listed in the Table. The most complete series are the *p*-toluidine and piperidine complexes where the effects of changing the ligands, L, may be compared, and the tri-*n*-propylphosphine complexes containing different amines.

All the compounds listed are beautifully crystalline. Those containing the lighter donor atoms, N, P, S, and Cl, are yellow with a trace of green or red, but the colours deepen towards red on ascending any group of donor atoms in the Periodic Table. This is most marked in the halide series, quite marked in the phosphorus group, but scarcely obvious with changing donor atoms of the sixth group. The complexes containing phosphines and phosphites as ligands, L, are qualitatively the most stable, but those containing a primary or a secondary amine, a 4-alkylpyridine, a sulphide, or an arsine are also very stable. The olefin and stibine complexes are less stable and in solution some of them decompose slowly with loss of the olefin and amine respectively. The selenide and telluride complexes tend to disproportionate, *e.g.*:

$$trans\text{-}[R_2Te,\ p\text{-}Me\cdot C_6H_4\cdot NH_2,PtCl_2] \longrightarrow (R_2Te)_2PtCl_2 + (p\text{-}Me\cdot C_6H_4\cdot NH_2)_2PtCl_2 \quad . \quad (5)$$

For this reason their *p*-toluidine complexes were obtained only in an impure state and are not recorded in the table. Nevertheless their piperidine analogues are sufficiently stable to be obtained pure. In contrast, the *p*-toluidine are more stable than the piperidine complexes when olefins or stibines constitute the ligand, L.

All the compounds listed dissolve readily in organic solvents except low-boiling petroleum. Generally solubilities increase in passing from phosphine to stibine, from

sulphide to telluride, and from chloro- to iodo-complexes. Also the complexes of the phosphorus group tend to be more soluble and to crystallise better than those of the sulphur group with an equal number of carbon atoms.

New complex compounds of the type trans-[L,amPtX$_2$]

(L = uncharged ligand, am = amine, X = halogen.)

L	am	X	M. p.	Colour
PEt_3	*p*-Toluidine	Cl	137·5—138·5°	Greenish-yellow
PBu^n_3	,,	,,	58·5—59·5	,,
$P(OEt)_3$	,,	,,	92—93	,,
Pr^n_2S	,,	,,	115—116·5	Orange-yellow
Bu^n_2S	,,	,,	85·5—87	,,
Bu^n_2S	,,	Br	98—98·5	Orange
4-*n*-Pentylpyridine	Piperidine	Cl	129·5—131	Greenish-yellow
PPr^n_3	,,	,,	125·5—127	,,
PPr^n_3	,,	Br	141—142	Deep yellow
PPr^n_3	,,	I	128·5—129·5	Deep orange
$P(OMe)_3$	,,	Cl	98—99	Greenish-yellow
$AsPr^n_3$	,,	,,	96·5—98	Mustard-yellow
$SbEt_3$	,,	,,	76—77	Yellowish-orange
Et_2S	,,	,,	71—72·5	Orange
Et_2Se	,,	,,	65—66·5	,,
Et_2Te	,,	,,	60·5—61·5	,,
PPr^n_3	NH_3	,,	99—99·5	Greenish-yellow
,,	$Me{\cdot}NH_2$	,,	58·5—59	,,
,,	$CH_2Ph{\cdot}NH_2$	,,	71—72	,,
,,	Et_2NH	,,	96—96·5	,,
,,	$Ph{\cdot}NH_2$	,,	120—120·5	,,
,,	*p*-$Cl{\cdot}C_6H_4{\cdot}NH_2$	,,	144—145	,,
,,	*p*-$NO_2{\cdot}C_6H_4{\cdot}NH_2$	,,	115—116·5	Yellow
,,	*p*-$Ph{\cdot}C_6H_4{\cdot}NH_2$	,,	129—130	Greenish-yellow
,,	*p*-$MeO{\cdot}C_6H_4{\cdot}NH_2$	,,	118—119	Yellow
,,	2 : 6-Dimethylaniline	,,	126—126·5	Greenish-yellow
,,	PhMeNH	,,	88·5—89·5	,,
,,	NH_3	I	62·5—63·5	Orange-red
4-*n*-Pentylpyridine	2 : 6-Dibromo-4-*n*-dodecylaniline	Cl	105—106	Greenish-yellow
4-*n*-Nonylpyridine	2 : 6-Dimethylaniline	,,	131·5—132·5	,,
PEt_3	$Et{\cdot}NH_2$	,,	63—64	,,
PBu^n_3	*o*-$Me{\cdot}C_6H_4{\cdot}NH_2$	,,	83—84·5	,,
Bu^n_2S	2 : 6-Dimethylaniline	,,	120·5—121·5	Deep yellow
$AsPr^n_3$	NH_3	,,	91—92	Mustard-yellow

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

The bridged complexes, $L_2Pt_2X_4$ (I), were prepared as described by Chatt and Venanzi (*loc. cit.*).

The bridge-splitting reaction (1) was usually carried out by treating one equivalent of $L_2Pt_2Cl_4$, dissolved or suspended in acetone, with two equivs. of amine at room temperature. In many cases reaction was immediate, but with the more insoluble bridged complexes the suspension was shaken for several hours to complete the reaction. This was generally accompanied by a lightening in colour. The solution was then taken to dryness under reduced pressure in the cold and the residue recrystallised. In many cases oils remained after the evaporation but generally they solidified on storage. In the worst cases the oils were induced to crystallise by dissolving them in ether and evaporating the solution in the cold under reduced pressure. The crude products were purified by recrystallisation from light petroleum (b. p. 60—80°) (charcoal). When a different procedure was necessary to split the bridge or to purify the products, this is described under the appropriate product below. The low yields are caused by the small scale of the reaction (2—3 g. of bridged complex) and high solubilities of the products in all organic solvents. All the products are non-electrolytes, as shown by conductivity experiments in nitrobenzene. Their molar conductivities were of the order 10^{-6} mho.

The *trans*-configurations of the products are evident from their solubilities in carbon tetrachloride, ether, and other non-polar solvents. Few of the corresponding *cis*-isomers are known but those known are much less soluble in non-polar solvents and are very much paler.

The *trans*-configuration of two typical members *trans*-[PEt_3,*p*-toluidine$PtCl_2$] and *trans*-[Et_2Se,piperidine$PtCl_2$] were checked by measuring their $\Delta\varepsilon/f$ in benzene solution ($\Delta\varepsilon$ = the increment in dielectric constant due to the solute, f = mol. fraction of solute). The values obtained were **40** and **54** respectively, which is reasonable for unsymmetrical compounds of *trans*-configuration. Symmetrical compounds of *cis*-configuration, *e.g.*, *cis*-$[(PPr^n_3)_2PtCl_2]$, have values of the order **160—170** (Chatt and Wilkins, *J.*, **1953**, 70).

The products from the bridge-splitting reactions were: trans-p-*Toluidinetriethylphosphinedichloroplatinum*, needles (from ethanol, then methanol) (yield, 40%) (Found: C, 31·7; H, 5·1. $C_{13}H_{24}NCl_2PPt$ requires C, 31·8; H, 4·9%).

trans-p-*Toluidinetri*-n-*butylphosphinedichloroplatinum*, needles (yield, 60%) (Found: C, 39·4; H, 6·3. $C_{19}H_{36}NCl_2PPt$ requires C, 39·6; H, 6·3%).

trans-p-*Toluidine*(*triethyl phosphite*)*dichloroplatinum* [prepared by adding *p*-toluidine in ethanol to a concentrated ethanolic solution of $\{P(OEt)_3\}_2Pt_2Cl_4$ then cooling to −70°; the product separated at once, was filtered off, and recrystallised from light petroleum] (yield, 30%) (Found: C, 29·0; H, 4·5. $C_{13}H_{24}O_3NCl_2PPt$ requires C, 29·05; H, 4·5%).

trans-p-*Toluidine*(*di*-n-*propyl sulphide*)*dichloroplatinum*, recrystallised from *cyclo*hexane, then benzene (yield, 20%) (Found: C, 32·0; H, 4·9. $C_{13}H_{29}NCl_2SPt$ requires C, 31·8; H, 4·7%).

trans-p-*Toluidine*(*di*-n-*butyl sulphide*)*dichloroplatinum* [oily and difficult to purify; spontaneous evaporation of its dichloromethane solution gave a product which recrystallised from light petroleum (b. p. 60—80°) in needles] (yield, 20%) (Found: C, 34·8; H, 5·3. $C_{15}H_{27}NCl_2SPt$ requires C, 34·7; H, 5·2%).

trans-p-*Toluidine*(*di*-n-*butyl sulphide*)*dibromoplatinum* (yield, 16%) (Found: C, 29·4; H, 4·4. $C_{15}H_{27}NBr_2SPt$ requires C, 29·6; H, 4·5%).

trans-*Piperidine*-4-n-*pentylpyridinedichloroplatinum*: (piperidine)$_2Pt_2Cl_4$ (2·4 g.) in acetone (50 c.c.) was boiled under reflux for 30 min. with 4-*n*-pentylpyridine (1·5 c.c.); the solution was then taken to dryness under reduced pressure and the *trans*-isomer extracted from the residue with boiling ether; the ethereal extract was then taken to dryness under reduced pressure and the pure product obtained in greenish-yellow needles by repeated recrystallisation of the residue from ethanol. The yield was 15% (Found: C, 36·1; H, 5·2. $C_{15}H_{24}N_2Cl_2Pt$ requires C, 36·0; H, 5·2; N, 5·6%); the *trans*-configuration was confirmed by Kurnakov's reaction with thiourea (*J. prakt. Chem.*, **1894**, **50**, 483; see also Chatt and Venanzi, *loc. cit.*). The ether-insoluble part from this bridge-splitting reaction was recrystallised from carbon tetrachloride and cis-*piperidine*-4-n-*pentylpyridinedichloroplatinum* obtained in pale yellow plates, m. p. 156—157° (yield, 8%) (Found: C, 35·9; H, 5·1; N, 5·7%); the *cis*-configuration was confirmed by Kurnakov's reaction. The very low yields of these pure *trans*- and *cis*-isomers were due to difficulties in purification, but from the initial crude separation with ether the *cis*-isomer appeared to predominate in the mixture. Where the bridge-splitting reaction was repeated at room temperature with the theoretical quantity of amine, reaction was not complete after 7 days but again both isomeric products were obtained.

trans-*Piperidinetri*-n-*propylphosphinedichloroplatinum*, prisms (yield, 25%) (Found: C, 32·9; H, 6·1. $C_{14}H_{32}NCl_2PPt$ requires C, 32·9; H, 6·3%).

trans-*Piperidinetri*-n-*propylphosphinedibromoplatinum* prisms (from ethanol) (yield, 30%) (Found: C, 27·9; H, 5·4. $C_{14}H_{32}NBr_2PPt$ requires C, 28·0; H, 5·4%).

trans-*Piperidinetri*-n-*propylphosphinedi-iodoplatinum*, prisms (from ethanol) (33%) (Found: C, 24·1; H, 4·6. $C_{14}H_{32}NI_2PPt$ requires C, 24·2; H, 4·6%).

trans-*Piperidine*(*trimethyl phosphite*)*dichloroplatinum*: $[P(OMe)_3]_2Pt_2Cl_4$ (2·5 g.), prepared by Schützenberger's method (*loc. cit.*, 1872), in methanol (10 c.c.) was treated with piperidine (0·6 c.c.) at −70°; the yellow precipitate was separated, washed with cold methanol, and dried; repeated recrystallisation from light petroleum (b. p. 60—80°) gave plate-like crystals of the pure *compound* (yield, 50%) (Found: C, 20·4; H, 4·2. $C_8H_{20}O_3NCl_2PPt$ requires C, 20·2; H, 4·2%).

trans-*Piperidinetri*-n-*propylarsinedichloroplatinum*, prisms (30%) (Found: C, 30·4; H, 5·65. $C_{14}H_{32}NCl_2AsPt$ requires C, 30·3; H, 5·8%).

trans-*Piperidinetriethylstibinedichloroplatinum*, prisms (20%) (Found: C, 23·45; H, 4·5. $C_{11}H_{26}NCl_2PtSb$ requires C, 23·6; H, 4·7%): this compound was readily purified in the normal manner when operations such as recrystallisation were carried out rapidly; nevertheless the infrared spectrum of its freshly prepared solution in carbon tetrachloride changed fairly rapidly with time, indicating spontaneous decomposition. The N–H band at 3235 cm.$^{-1}$ due to the complex decreased in intensity with time, whilst a new band appeared at 3177 cm.$^{-1}$.

trans-*Piperidine(diethyl sulphide)dichloroplatinum*, plates [from *cyclo*hexane, then light petroleum (b. p. 60—80°)] (30%) (Found : C, 24·35; H, 4·8. $C_9H_{21}NCl_2SPt$ requires C, 24·5; H, 4·8%).

trans-*Piperidine(diethyl selenide)dichloroplatinum*, plates (14%) (Found : C, 22·1; H, 4·3. $C_9H_{21}NCl_2PtSe$ requires C, 22·1; H, 4·3%).

trans-*Piperidine(diethyl telluride)dichloroplatinum*, plates (30%) (Found : C 20·4; H, 4·0. $C_9H_{21}NCl_2PtTe$ requires C, 20·1; H, 3·9%).

trans-*Amminotri*-n-*propylphosphinedichloroplatinum* (prepared in ethanol), plates (60%) (Found : C, 24·6; H, 5·5; N, 3·3. $C_9H_{24}NCl_2PPt$ requires C, 24·4; H, 5·6; N, 3·2%).

trans-*Methylaminetri*-n-*propylphosphinedichloroplatinum*, obtained as an oil and induced to crystallise by keeping its concentrated ethanol solution at −70° for 15 hr., and purified by partial evaporation of its light petroleum (b . p. 40—60°) solution from which it separated in prisms (30%) (Found : C, 26·2; H, 5·6. $C_{10}H_{26}NCl_2PPt$ requires C, 26·3; H, 5·7%).

trans-*Benzylaminetri*-n-*propylphosphinedichloroplatinum*, plates (50%) (Found : C, 36·0; H, 5·6. $C_{16}H_{30}NCl_2PPt$ requires C, 36·0; H, 5·7%).

trans-*Diethylaminetri*-n-*propylphosphinedichloroplatinum*, plates (from methanol) (85%) (Found : C, 31·3; H, 6·4. $C_{13}H_{32}NCl_2PPt$ requires C, 31·3; H, 6·5%).

trans-*Anilinetri*-n-*propylphosphinedichloroplatinum*, needles from ethanol (yield, 35%) (Found : C, 34·3; H, 5·3; N, 3·0. $C_{15}H_{28}NCl_2PPt$ requires C, 34·7; H, 5·4; N, 2·7%).

trans-p-*Chloroanilinetri*-n-*propylphosphinedichloroplatinum*, plates from methanol (yield, 30%) (Found : C, 32·5; H, 4·85; N,2·7. $C_{15}H_{27}NCl_3PPt$ requires C, 32·5; H, 4·9; N, 2·5%).

trans-p-*Nitroanilinetri*-n-*propylphosphinedichloroplatinum*, plums from ethanol (yield, 25%) (Found : C, 31·7; H, 4·7. $C_{15}H_{27}O_2N_2Cl_2PPt$ requires C, 31·9; H, 4·8%).

trans-4-*Diphenylylaminetri*-n-*propylphosphinedichloroplatinum*, needles from ethanol (yield, 40%) (Found : C, 42·1; H, 5·5. $C_{21}H_{32}NCl_2PPt$ requires C, 42·35; H, 5·4%).

trans-p-*Anisidinetri*-n-*propylphosphinedichloroplatinum*, prisms from methanol (yield, 50%) (Found : C, 34·7; H, 5·6; N, 2·8. $C_{16}H_{30}ONCl_2PPt$ requires C, 35·0; H, 5·5; N, 2·55%).

trans-2 : 6-*Dimethylanilinetri*-n-*propylphosphinedichloroplatinum*, needles (40%) (Found : C, 37·0; H, 5·9. $C_{17}H_{32}NCl_2PPt$ requires C, 37·3; H, 5·9%).

trans-N-*Methylanilinetri*-n-*propylphosphinedichloroplatinum*, prisms from methanol (yield, 25%) (Found : C, 36·1; H, 5·6. $C_{16}H_{30}NCl_2PPt$ requires C, 36·0; H, 5·7%).

trans-*Amminotri*-n-*propylphosphinedi-iodoplatinum* : its chloro-analogue (2 g.) in acetone (50 c.c.) was shaken for several hours with finely divided potassium iodide (1·6 g.); the red solution was filtered and taken to dryness under reduced pressure; the residual oil, which solidified on storage, was extracted with light petroleum (b. p. 40—60°) [the residue was $(PPr^n_3)_2Pt_2I_4$, m. p. 185—190°, alone and mixed with an authentic specimen]; the light petroleum solution was taken to dryness under reduced pressure and the residual solid repeatedly crystallised from light petroleum (b. p. 40—60°) forming prisms (yield, 35%) (Found : C, 17·3; H, 3·85. $C_9H_{24}NI_2PPt$ requires C, 17·3; H, 3·9%).

trans-4-n-*Pentylpyridine*-2 : 6-*dibromo*-4-n-*dodecylanilinedichloroplatinum*, prepared by shaking a suspension of the pentylpyridine-bridged complex and the aniline in ethanol until all had dissolved to a yellow solution, was isolated in the usual manner and recrystallised from ethanol in plates (20%) (Found : C, 40·2; H, 5·2; N, 3·4. $C_{28}H_{44}N_2Cl_2Br_2Pt$ requires C, 40·3; H, 5·3; N, 3·4%). The reaction of formation appears to be reversed in carbon tetrachloride because the infrared spectrum of the above mixed complex in carbon tetrachloride solution showed the slow development of absorption bands at 3490 and 3392 cm.$^{-1}$ attributable to free 2 : 6-dibromo-4-*n*-dodecylaniline.

trans-4-n-*Nonylpyridine*-2 : 6-*dimethylanilinedichloroplatinum* (similarly prepared), needles from ethanol (yield, 20%) (Found : C, 44·6; H, 6·3; N, 4·9. $C_{22}H_{34}N_2Cl_2Pt$ requires C, 44·6; H, 5·8; N, 4·7%).

trans-*Ethylaminetriethylphosphinedichloroplatinum*, needles (50%) (Found : C, 22·7; H, 5·2. $C_8H_{22}NCl_2PPt$ requires C, 22·4; H, 5·2%).

trans-o-*Toluidinetri*-n-*butylphosphinedichloroplatinum*, needles (30%) (Found : C, 39·5; H, 6·1. $C_{19}H_{38}NCl_2PPt$ requires C, 39·6; H, 6·3%).

trans-2 : 6-*Dimethylaniline*(*di*-n-*butyl sulphide*)*dichloroplatinum*, needles (40%) (Found : C, 36·3; H, 5·4; N, 3·0; S, 6·1. $C_{16}H_{29}NCl_2SPt$ requires C, 36·0; H, 5·5; N, 2·6; S, 6·0%).

trans-*Amminotri*-n-*propylarsinedichloroplatinum*, plates (yield, 75%) (Found : C, 22·3; H, 4·8. $C_9H_{24}NCl_2AsPt$ requires C, 22·2; H, 5·0%).

An attempt to prepare *trans*-piperidine(di-*n*-propyl sulphide)dichloroplatinum by the bridge-splitting reaction led to an oil. Treatment with a further two mols. of piperidine caused slow

separation of *dipiperidine(di-n-propyl sulphide)chloroplatinum chloride* [$pip_2PPr^n_3PtCl$]Cl, of unknown, but probably *cis*-, configuration. It was purified by washing it with light petroleum (b. p. 60—80°) and repeated recrystallisation from carbon tetrachloride. The salt formed white prisms, melting at 122—123·5° to a yellow oil (Found: C, 34·6; H, 6·5; N, 5·2. $C_{16}H_{36}N_2Cl_2SPt$ requires C, 34·6; H, 6·5; N, 5·05%).

Attempts to prepare trans-*Diphenylaminetri*-n-*propylphosphinedichloroplatinum.*—$(PPr^n_3)_2Pt_2Cl_4$ (0·5 g.) in benzene (50 c.c.) was treated with diphenylamine (0·7 g.). There was no colour change but on evaporating the benzene a partly crystalline residue remained. Its ethanol solution deposited orange crystals, which after one recrystallisation from acetone had m. p. 179—181° alone and mixed with $(PPr^n_3)_2Pt_2Cl_4$ of m. p. 182°. $(PPr^n_3)_2Pt_2Cl_4$ is almost insoluble in carbon tetrachloride but dissolves more readily in presence of diphenylamine (2 mols.); however, the desired product cannot be isolated from the solution. That reaction occurred between the bridged complex and diphenylamine was also shown by decrease in the intensity of the N–H stretching band of the free amine at 3433 cm.$^{-1}$ on addition of the bridged complex to a carbon tetrachloride solution of the amine, whilst another broader band appeared at 3214 cm.$^{-1}$, probably due to the complex $[Ph_2NH,PPr^n_3PtCl_2]$.

Reaction 3.—$(Piperidine)_2Pt_2Cl_4$ (0·42 g.) in chloroform (50 c.c.) was shaken in an ethylene atmosphere. A solid slowly separated during about 18 hr. This was recrystallised from ethyl methyl ketone (charcoal), to give pure cis-*piperidine-ethylenedichloroplatinum* in yellowish-white needles, decomp. 180—185° (yield, 77%) (Found: C, 22·4; H, 4·05. $C_7H_{15}NCl_2Pt$ requires C, 22·2; H, 4·0%). This is very much less soluble in organic solvents than its *trans*-isomer (Chatt and Venanzi, *loc. cit.*).

Reaction 4.—This is described by Chatt and Venanzi (*loc. cit.*).

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Colchicine and Related Compounds. Part XIV. Structure of β- and γ-Lumicolchicine.*

By E. J. Forbes.

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The action of sunlight on dilute aqueous solutions of colchicine leads to the formation of α-, β-, and γ-lumicolchicine, each isomeric with colchicine (Grewe and Wulf, *Chem. Ber.*, 1951, **84**, 621). Degradative and spectroscopic evidence suggests that β- and γ-lumicolchicine are stereoisomers and indicates that they have tetracyclic structures which arise from a rearrangement of the bonds in the tropolone ring of colchicine.

It has been known for some time that colchicine (I) and its solutions undergo some change when exposed to sunlight (Hübler, *Arch. Pharm.*, 1865, **171**, 205; Struve, *Z. anal. Chem.*, 1873, **12**, 164). Jacobi (*Arch. exp. Path. Pharmak.*, 1890, **27**, 129) isolated an amorphous product, which, by reason of its analysis, he called oxydicolchicine. These experiments were probably concerned mainly with photo-oxidation, since air was invariably present. Later, it was shown (Macht, *Science*, 1927, **66**, 653) that only the short-wave portion of sunlight was capable of effecting any change. By irradiating solutions of colchicine in water with a powerful source of ultraviolet light, Grewe (*Naturwiss.*, 1946, **33**, 187) was able to effect a photo-isomerisation, which gave a small quantity of crystalline material. When very dilute solutions of pure colchicine were exposed to the available sunlight for 5—7 weeks, air being excluded from the system, there was obtained an almost theoretical yield of transformation product (Grewe and Wulf, *Chem. Ber.*, 1951, **84**, 621). This

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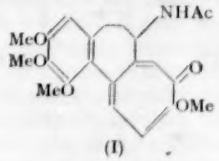
material was separated into three crystalline substances designated α-, β-, and γ-lumicolchicine, each isomeric with colchicine.

Concurrently, Šantavý (*Coll. Czech. Chem. Comm.*, 1951, **16**, 655), using less defined conditions, obtained " lumicolchicine " I by the action of sunlight on aqueous solutions of colchicine and " lumicolchicines " I and II by the action of ultraviolet radiations. In fact, lumicolchicines I and II are identical with the β- and the γ-isomer isolated by Grewe and Wulf (Šantavý, *loc. cit.*). It is of interest that these two compounds are identical with substances I and J, which are obtained, along with colchicine, from the meadow saffron, *Colchicum autumnale* (*idem*, *loc. cit.*), since it provides an example of a transformation which sunlight is capable of effecting in the plant, presumably without the connivance of enzymes.

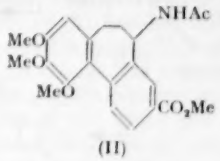
In the present work, dilute solutions of colchicine in water, under an atmosphere of nitrogen, were exposed to summer sunlight during 8—10 weeks. The transformation product was separated by fractional crystallisation from methanol into three isomeric compounds whose properties are in excellent agreement with those recorded for α-, β-, and γ-lumicolchicine by Grewe and Wulf (see Experimental section). They obtained the three isomers in roughly comparable amounts whereas here there was formed a preponderance of β-lumicolchicine, the other isomers being present in much smaller amounts. This discrepancy may well be due to a difference in the actinic value of the incident sunlight or to the different transparencies, toward ultraviolet light, of the glass of the containing vessels.

The near identity of the ultraviolet spectra (maxima at 225, 266, and 340 mμ) of β- and γ-lumicolchicine, together with the close resemblance of their infrared curves in the higher-frequency region, suggests a stereochemical rather than a structural relation between them, and this paper seeks to present a body of facts in favour of this assignment.

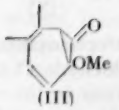
It was shown (Grewe and Wulf, *loc. cit.*) that on catalytic hydrogenation with Adams catalyst at atmospheric pressure, β- and γ-lumicolchicine absorbed only two mols. of hydrogen to give tetrahydro-compounds, in contrast to colchicine which forms a hexhydro-derivative (Bursian, *Ber.*, 1938, **71**, 245; Kemp and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 243). Further, it was shown (Grewe and Wulf, *loc. cit.*) that these tetrahydro-compounds absorbed rapidly only one atom of oxygen when titrated with perbenzoic acid, indicating the presence of one remaining aliphatic double bond, so that these compounds contain a fourth ring. Such a transformation (apart from any others which might have occurred) is most easily envisaged as a rearrangement of the bonds of the tropolone ring. On this basis, if stereochemical considerations are ignored, three structures (III—V) are possible. In each the extended conjugation of the colchicine molecule has been interrupted,



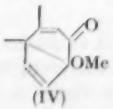
(I)



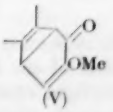
(II)



(III)



(IV)



(V)

requiring a shift of some of the light absorption maxima to shorter wavelengths. Indeed for β- and γ-lumicolchicine the intense maxima are located at 228 and 266 mμ (shoulder at 280 mμ) as against 247 and 350 mμ in colchicine. Moreover β- and γ-lumicolchicine show carbonyl activity as required by these tetracyclic structures. In addition to simple oximes and semicarbazones, they form osazones and dioximes (in pyridine), the latter by the loss of a methoxyl group. The dioximes react with nickel and copper salts to form brown and green complexes which are soluble in chloroform.

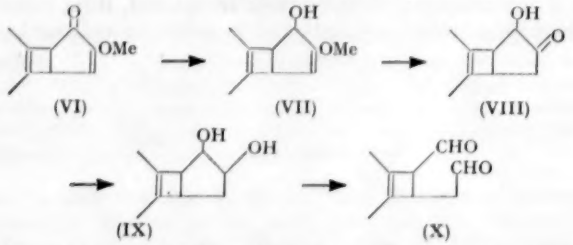
The usual methods of attack on the tropolone moiety of the colchicine molecule proved ineffectual when applied to β- and γ-lumicolchicine, *e.g.*, sodium methoxide in methanol [under more vigorous conditions than are required to rearrange colchicine to *allo*colchicine (II)], and very dilute acid at 100°. Stronger acid hydrolysed simultaneously the methoxyl and the amide group, and led to intractable products.

β-Lumicolchicine was smoothly reduced by sodium borohydride in methanol to a dihydro-compound, which contains four methoxyl groups and forms a monoacetate, but not an oxime. Its infrared spectrum shows no absorption in the carbonyl region other than that due to the amide group at 1642 cm.$^{-1}$.

At 100° N-hydrochloric acid hydrolysed dihydro-β-lumicolchicine almost instantaneously to demethyldihydro-β-lumicolchicine, $C_{21}H_{25}O_6N$, which contains only three methoxyl groups and forms a monoacetate and, moreover, an oxime. Its infrared absorption curve shows a peak at 1742 cm.$^{-1}$ (carbonyl stretching) in addition to that at 1654 cm.$^{-1}$ (amide CO). The ready hydrolysis of the methoxyl group indicates its presence as an enol ether. This points to formula (V) for β-lumicolchicine and precludes (III) and (IV) which are aliphatic ethers, as would be the dihydro-derivatives obtained by reduction of the keto-group. Structure (V) incorporates the monoenol ether of a 1 : 2-diketone and is consistent with the fact that the hydrolysis of β-lumicolchicine is less easy than that of dihydro-β-lumicolchicine, since the competition of the keto-group for the available hydrogen ions no longer pertains in the derived hydroxy-compound. These reactions may now be represented by partial formulæ (VI)—(VIII).

As required by structure (VIII), demethyldihydro-β-lumicolchicine has the properties of an acyloin. It reduced Fehling's solution and formed osazones with phenylhydrazine and its derivatives. In fact the 2 : 4-dinitrophenylosazone was identical with that obtained directly from β-lumicolchicine, by the loss of a methoxyl group, thus showing that the molecule had undergone no skeletal rearrangement during the previous stages. In addition demethyldihydro-β-lumicolchicine formed a dioxime, which differed from the two isomeric dioximes obtained from β-lumicolchicine (by the loss of a methoxyl group) and is presumably the third of the four possible isomers (see Experimental section).

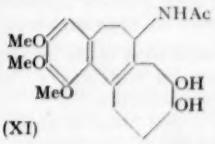
Demethyldihydro-β-lumicolchicine was reduced in aqueous methanol by sodium borohydride to a 1 : 2-glycol (IX), which showed no carbonyl absorption in the infrared other than that of the amide group. This glycol was not separated into its stereoisomers but straightway oxidised with sodium metaperiodate in aqueous ethanol at pH 7—the use of periodic acid led to side reactions. The product, which gave a positive Angeli–Rimini



(VI) (VII) (VIII) (IX) (X)

reaction for an aldehyde, was isolated as its 2 : 4-dinitrophenylhydrazone, whose analysis corresponded to that of the bis-derivative of the dialdehyde (X). The bis-2 : 4-dinitrophenylhydrazone is light orange and shows a maximum in the ultraviolet spectrum at 353 mμ, both features characteristic of the derivative of a saturated carbonyl compound as required by (X). The formation of a dialdehyde, which does not undergo ring-closure under the acidic conditions of dinitrophenylhydrazone formation, is compatible with structure (X) and may be cited as evidence for the formation of a bridge across ring C of the colchicine molecule during its photoisomerisation. Had this not occurred the resultant 1 : 7-dialdehyde would almost certainly have suffered internal aldol condensation to give a monoaldehyde as occurs when hexahydrocolchicine (XI) is treated similarly (Arnstein, Tarbell, Scott, and Huang, *J. Amer. Chem. Soc.*, 1949, **71**, 2448).

The possibility of a second double bond (not susceptible to hydrogenation at atmospheric pressure), instead of a fourth ring, in demethyldihydro-β-lumicolchicine (VIII) was precluded by the result of titrating its acetate with a molar excess of monoperphthalic acid in chloroform: only 1·15 atoms of oxygen (as determined by iodine–thiosulphate titration) were absorbed in 24 hr., indicating the presence of only one aliphatic double bond. The epoxide could not be obtained crystalline.



(XI)

Micro-hydrogenation of demethyldihydro-β-lumicolchicine and its acetate gave some support for their tetracyclic nature. With Adams catalyst in acetic acid, the acetate absorbed one mol. of hydrogen as required for the carbonyl group; but demethyldihydro-β-lumicolchicine surprisingly absorbed two mols. of hydrogen, a result which is not easy to explain: hydrogenolysis of the hydroxyl group and rupture of the *cyclo*butenering are possibilities. When palladium was substituted for Adams catalyst neither demethyldihydro-β-lumicolchicine nor its acetate absorbed hydrogen, compatibly with formula (VIII) for the acyloin.

γ-Lumicolchicine undergoes an analogous series of reactions which yield compounds whose chemical properties closely resemble those of the β-isomer. On reduction with sodium borohydride in aqueous methanol, γ-lumicolchicine yielded a dihydro-compound which contains four methoxyl groups and forms an acetate. Dihydro-γ-lumicolchicine was readily hydrolysed by dilute acid to demethyldihydro-γ-lumicolchicine, $C_{21}H_{25}O_6N$, which contains only three methoxyl groups and shows the properties of an acyloin. When treated with sodium borohydride demethyldihydro-γ-lumicolchicine was reduced to a glycol, which was then cleaved by sodium metaperiodate at pH 7. The resulting carbonyl compound was isolated as its 2 : 4-dinitrophenylhydrazone whose analysis showed the presence of two carbonyl groups. This derivative was orange and showed an ultraviolet maximum at 356 mμ, both characteristic of a saturated carbonyl compound. As expected, its ultraviolet spectrum closely resembles that of the corresponding β-derivative but their melting-point behaviour establishes their non-identity Further, when treated with an excess of monoperphthalic acid in chloroform, demethyldihydro-γ-lumicolchicine acetate took up only one atom of oxygen, corresponding to one double bond. These results indicate that γ-lumicolchicine is a tetracyclic compound and that, by the same arguments as those cited for the β-isomer, it may be represented by (V), but not (III) or (IV). The sequence of reactions may again be interpreted by partial formulæ (VI)—(X).

Thus, with the assumption that no photochemical change has occurred in colchicine other than the bridging of the tropolone ring, β- and γ-lumicolchicine may be assigned a stereochemical relation which involves the two forms of (V) which can be obtained by *cis*-fusion of the four- and five-membered rings (*trans*-fusion would result in excessive strain in the *cyclo*butene ring); so that if ring A, ring B, and the four-membered ring are considered as a planar system, from the point of view of stereoisomerism, the acetamido-group and the fused five-membered ring would be either *cis* or *trans* to one another. If, in addition, the optically active centre in colchicine has been involved in the transformation, then the enantiomorphic forms of the *cis*- and the *trans*-isomer already mentioned become possible structures; so that β- and γ-lumicolchicine may be either geometrical isomers or a pair of enantiomorphs.

For the rest of the molecule only certain features are clear. Ring A and its junction with ring C in the colchicine molecule have remained intact, as is shown by the isolation of 3 : 4 : 5-trimethoxyphthalic anhydride on permanganate oxidation of β-lumicolchicine. The acetamido-group as in colchicine is clearly indicated by the infrared spectrum of both β- and γ-lumicolchicine, and an almost quantitative *C*-methyl determination.

The size of ring B cannot be inferred from any of the above reactions, but the close

similarity of the ultraviolet spectra of the dihydro-compounds, which concerns only ring A and the attendant conjugation in ring B—both show maxima at 230 and 280 mμ—suggests that it is the same in both isomers. Work is in progress to elucidate this point, to obtain direct evidence for the size of the other rings and to determine the configuration of the point of attachment of the acetamido-side-chain.

Experimental

Irradiation of Colchicine and Separation of the Products.—The irradiations were carried out according to the directions of Grewe and Wulf (*loc. cit.*) with some modifications: the separation of the products followed a different procedure.

Colchicine (5 g.) was dissolved in hot distilled water (2 l. at 80°) through which a stream of nitrogen was being passed. The solution was poured, whilst still hot, into cylindrical tubes (90 × 5 cm.) which were sealed immediately under nitrogen. After 10 days' exposure on the roof of the laboratory, the solution began to deposit crystals. These had a characteristic needle shape and grew steadily for about 3—4 weeks; then the edges began to lose their form. About this time the solution deposited a light amorphous precipitate which grew until it filled the whole of the liquid. After 8—10 weeks, depending upon the amount of sunshine, the tubes were opened and the contents worked up as follows.

The solutions were filtered (filtrate A), and the solid was washed with water and dried at room temperature. The dried material (14 g. from 20 g. of colchicine) was finely powdered and suspended in boiling methanol (150 c.c.) for 15 min.; the hot solution was filtered. After being washed with methanol, the residue (1·0 g.) consisted of almost pure α-lumicolchicine. A further crop (0·05 g.) was obtained from the mother-liquors on cooling. One recrystallisation from ethanol afforded colourless needles, m. p. 165°, $[\alpha]_D$ +80° (*c* 0·53 in $CHCl_3$) (Found: C, 63·2; H, 6·5; N, 3·5; OMe, 29·3. Calc. for $C_{22}H_{25}O_6N,H_2O$: C, 63·3; H, 6·5; N, 3·4; 4OMe, 29·7%). Grewe and Wulf (*loc. cit.*) give m. p. 165°, $[\alpha]_D$ +81°.

After removal of α-lumicolchicine, the solution was concentrated to 75 c.c. and left overnight. The wool-like precipitate which had formed was then filtered off and washed with ethanol. It consisted of long slender needles of pure γ-lumicolchicine (1·1 g.), m. p. 272° (decomp.), $[\alpha]_D$ −434° (*c* 0·66 in $CHCl_3$) [Found: C, 66·0; H, 6·2; N, 3·7; OMe, 31·1%; *M* (Rast, in camphorquinone), 416. Calc. for $C_{22}H_{25}O_6N$: C, 66·2; H, 6·3; N, 3·5; OMe, 31·1%; *M*, 399]. Grewe and Wulf (*loc. cit.*) give m. p. 268°, $[\alpha]_D$ −445°.

Further concentration of the mother-liquors yielded successive fractions of β-lumicolchicine of different m. p.s owing to a mixture of two crystalline forms. The first fractions consisted of the high-melting form, m. p. 204—205°; these were followed by intermediate fractions, m. p. 198—202°, which invariably softened at about 180°; finally there was a fraction of the lower-melting form, m. p. 179—180°. All fractions showed much the same optical rotation, indicating that they consisted of almost pure β-lumicolchicine. The combined yield was 10·7 g. Recrystallisation from aqueous ethanol afforded the higher-melting form in long needles, m. p. 206°: the lower-melting form was obtained from ethyl acetate–ethanol in rosettes of needles, m. p. 181°. Both gave $[\alpha]_D$ +308° (*c* 0·53 in $CHCl_3$) [Found: C, 66·1; H, 6·5; OMe, 31·1%; *M* (Rast), 410]. Grewe and Wulf (*loc. cit.*) give m. p. 183° and 207°, $[\alpha]_D$ +309°.

Extraction of filtrate A with ethyl acetate afforded a further quantity (4·0 g.) of β-lumicolchicine, m. p. 179—180°. A final extraction with chloroform yielded, first, γ-lumicolchicine (0·2 g.; m. p. 265—267°) followed by β-lumicolchicine (1·1 g.; m. p. 204—205°).

Total yields were: α-, 1·05 g., β-, 15·8 g., and γ-lumicolchicine, 1·3 g. Grewe and Wulf (*loc. cit.*) record yields in the ratios 4 : 3 : 2.

β-Lumicolchicine oxime was prepared in aqueous alcohol by hydroxylamine hydrochloride and sodium acetate. It crystallised from aqueous ethanol in fine matted needles, m. p. 263° (decomp.) (Found: C, 63·5; H, 6·3; N, 7·2. Calc. for $C_{22}H_{26}O_6N_2$: C, 63·7; H, 6·3; N, 6·8%). Šantavý (*loc. cit.*) records m. p. 274—276° (corr.).

The *dioxime* of demethyl-β-lumicolchicine was obtained when a solution of β-lumicolchicine (200 mg.) and hydroxylamine hydrochloride (100 mg.) in ethanol (1 c.c.) and pyridine (2 c.c.) was heated under reflux for 2 hr. After removal of solvents the residue was triturated with methanol, affording the solid *dioxime*, which crystallised from methanol in colourless plates, m. p. 184—186° (Found: C, 58·4; H, 6·4; N, 9·7. $C_{21}H_{25}O_6N_3,H_2O$ requires C, 58·2; H, 6·2; N, 9·7%). The mother-liquors afforded an *isomer* which crystallised from ethanol in small colourless needles, m. p. 233—234° (Found: C, 58·5; H 5·7%).

γ-Lumicolchicine oxime, prepared in aqueous ethanol, crystallised from aqueous ethanol in silky needles, m. p. 284—286° (decomp.) (Found: C, 63·8; H, 6·3; N, 6·9%). Šantavý (*loc. cit.*) records m. p. 309—311° (corr.).

2 : 4-*Dinitrophenylosazone of Demethyl-β-lumicolchicine.*—A warm solution of 2 : 4-dinitrophenylhydrazine (30 mg.) in methanol (3 c.c.) containing a drop of concentrated hydrochloric acid was added to a solution of β-lumicolchicine (30 mg.) in methanol (2 c.c.). After 15 min. the deep red crystalline precipitate was collected, washed with methanol, and recrystallised from nitromethane. The *osazone* was deposited overnight in deep-red feathery needles, m. p. 212° (Found: C, 52·8; H, 4·2; N, 16·8. $C_{33}H_{39}O_{12}N_9$ requires C, 53·2; H, 4·0; N, 17·0%). Light absorption: $\lambda_{max.}$ at 221, 270, 355, and 452 mμ.

Oxidation of β-Lumicolchicine.—A suspension of β-lumicolchicine (0·5 g.) in 5% aqueous potassium hydroxide (5 c.c.) and acetone (5 c.c.) was treated with a 4% solution of potassium permanganate (25 c.c.). When the colour had almost disappeared the mixture was heated on a steam-bath for 2 hr. During this time a concentrated solution of potassium permanganate (7 g.) in water (35 c.c.) was added gradually. The resulting solution, which was still pink, was acidified, whilst hot, with dilute sulphuric acid. When the effervescence had subsided, the mixture was rendered alkaline and filtered from manganese dioxide. The straw-coloured filtrate was acidified and extracted with ethyl acetate (3 × 25 c.c.). The combined extracts were dried, the solvent was removed, and the residue sublimed at 160°/0·2 mm., giving a pale yellow solid, which was taken up in ether and treated with charcoal. After removal of the ether, the residue was sublimed at 120°/0·2 mm., giving a colourless solid (50 mg.) which, on crystallisation from ether or carbon tetrachloride, afforded 3 : 4 : 5-trimethoxyphthalic anhydride as needles, m. p. and mixed m. p. 144° (Found: C, 55·8; H, 4·7. Calc. for $C_{11}H_{10}O_6$: C, 55·5; H, 4·2%).

Dihydro-β-lumicolchicine (VII).—A solution of β-lumicolchicine (500 mg.) and sodium borohydride (50 mg.) in methanol (15 c.c.) was set aside overnight. Dilute acid was then added until the solution was neutral to B.D.H. universal-indicator paper, and the bulk of the solvent was removed *in vacuo*. Addition of water to the residue produced a crystalline prepipitate of *dihydro-β-lumicolchicine* (460 mg.), which crystallised from aqueous ethanol in colourless prisms, m. p. 195° (Found: C, 65·6; H, 6·4; N, 3·7. $C_{22}H_{27}O_6N$ requires C, 65·8; H, 6·7; N, 3·5%).

The *acetate*, prepared in acetic anhydride and a large excess of pyridine, crystallised from aqueous ethanol in needles, m. p. 221° (Found: C, 64·7; H, 6·3; OMe, 27·8. $C_{24}H_{29}O_7N$ requires C, 65·0; H, 6·6; 4OMe, 28·0%).

Dihydro-γ-lumicolchicine (VII).—A solution of sodium borohydride (25 mg.) in water (1 c.c.) was added to a suspension of γ-lumicolchicine (100 mg.) in methanol (4 c.c.). After 1 hr. the solid had dissolved, and the solution was left overnight. After the solution had been brought to pH 7, the bulk of the solvent was removed *in vacuo*; a viscous oil separated. After addition of water, the aqueous layer was decanted, and the residual gum boiled with water. After a minute it had completely solidified and was removed (76 mg.). On crystallisation from aqueous ethanol it afforded *dihydro-γ-lumicolchicine* in rosettes of colourless needles, m. p. 204° (Found: C, 65·6; H, 6·8; N, 3·7%).

Demethyldihydro-β-lumicolchicine (VIII).—N-Hydrochloric acid (5 c.c.), previously heated to 100°, was added in one portion to a solution of dihydro-β-lumicolchicine (200 mg.) in hot ethanol (0·75 c.c.), giving a clear solution which began to deposit crystals after a few seconds. After 30 min. the crystals (177 mg.) were separated and crystallised from aqueous ethanol, whence *demethyldihydro-β-lumicolchicine* was obtained in colourless blades, m. p. 208° (Found: C, 65·2; H, 6·6; N, 3·7; OMe, 23·8. $C_{21}H_{25}O_6N$ requires C, 65·1; H, 6·5; N, 3·6; 3OMe, 24·0%).

The *acetate*, prepared in pyridine, crystallised from benzene–light petroleum in plates, m. p. 192° (Found: C, 64·4; H, 6·3. $C_{23}H_{27}O_7N$ requires C, 64·3; H, 6·3%). The *oxime*, prepared in aqueous alcohol, crystallised from the same solvent in short colourless needles, m. p. 238° (Found: C, 62·7; H, 6·4; N, 7·3. $C_{21}H_{26}O_6N_2$ requires C, 62·9; H, 6·5; N, 7·0%). The dinitrophenylosazone (prepared as for β-lumicolchicine) crystallised from nitromethane in deep-red feathery needles, m. p. 212° alone and when mixed with the osazone from β-lumicolchicine. Light absorption in EtOH: $\lambda_{max.}$ at 221, 270, 355, and 452 mμ. The *dioxime*, prepared in pyridine, was obtained from ethanol in colourless needles, m. p. 175—176° (Found: N, 9·6. $C_{21}H_{25}O_6N_3,H_2O$ requires N, 9·7%).

Demethyldihydro-γ-lumicolchicine (VIII).—Dihydro-γ-lumicolchicine (200 mg.) in ethanol (1 c.c.) was treated with N-hydrochloric acid (4 c.c.) previously heated to 100°. The clear

solution so produced slowly deposited *demethyldihydro-γ-lumicolchicine* on cooling. It crystallised from aqueous ethanol in massive prisms, m. p. 238° (Found: C, 65·1; H, 6·4; OMe, 24·1%).

The *acetate*, prepared in acetic anhydride–pyridine, crystallised from ethyl acetate–light petroleum (b. p. 80—100°) in flat needles, m. p. 237° (Found: C, 64·3; H, 6·3%). The *oxime*, prepared in aqueous ethanol, crystallised from benzene–ethanol in small needles, m. p. 193° (Found: N, 6·8%).

Treatment of Demethyldihydro-β- and -γ-lumicolchicine Acetates with Monoperphthalic Acid.—Demethyldihydro-β-lumicolchicine acetate (157 mg.) in chloroform (10 c.c.) was treated with monoperphthalic acid in chloroform (4 c.c. containing 0·1364 g.). The volume was made up to 25 c.c., and the solution set aside at 0°. After 24 hr. the consumption of peracid, determined by iodine–thiosulphate titration, was 77 mg., corresponding to 1·15 mols. The chloroform solution afforded only a gum.

Similarly demethyldihydro-γ-lumicolchicine acetate (68 mg.) in chloroform (3 c.c.) was treated with monoperphthalic acid in chloroform (1·5 c.c. containing 51·1 mg.), the volume then being made up to 10 c.c. After 24 hr. the consumption of peracid was 32 mg. (1·1 mols.). Working up the solution did not give a crystalline epoxide.

Reduction of Demethyldihydro-β-lumicolchicine with Sodium Borohydride.—A solution of sodium borohydride (20 mg.) in water (1 c.c.) was added to a suspension of demethyldihydro-β-lumicolchicine (100 mg.) in methanol (2 c.c.). After 15 min. dissolution was complete, and the mixture was left overnight. After addition of acid to pH 7, the solution was evaporated under reduced pressure to a small bulk. Addition of a saturated solution of sodium sulphate in water (5 c.c.) then precipitated the glycol (IX) as a gum, which was extracted with chloroform (3 × 10 c.c.). The combined chloroform extracts were dried and evaporated, and the residual gum was taken up in benzene (5 c.c.). After removal of the benzene the glycol which remained as a colourless glass was not separated into its stereoisomers.

Periodate Oxidation of the Glycol from Demethyldihydro-β-lumicolchicine.—A solution of the glycol, prepared as above, in methanol (2 c.c.) was treated with one of sodium metaperiodate (55 mg., 1 mol.) in water (2 c.c.). After 48 hr., the solution was diluted with water (10 c.c.) and extracted with chloroform (3 × 10 c.c.). The combined chloroform extracts were dried and evaporated, and the residual gum was taken up in ethanol (1 c.c.)—this solution gave a positive Angeli–Rimini test for an aldehyde group. On addition of 2 : 4-dinitrophenylhydrazine (150 mg.) in methanol (5 c.c.) containing a drop of concentrated hydrochloric acid, a red crystalline precipitate was slowly formed. After 2 hr., the solid was collected, washed with methanol, and recrystallised from glacial acetic acid. The *bis*-2 : 4-*dinitrophenylhydrazone* of the dialdehyde (X) was thereby obtained in clusters of orange needles, m. p. 150° after drying for 4 hr. at 110°/1 mm. (Found: C, 52·9; H, 4·2; N, 16·7. $C_{33}H_{31}O_{12}N_9$ requires C, 53·1; H, 4·2; N, 16·8%). Light absorption in EtOH: $\lambda_{max.}$ 353 mμ.

Reduction of Demethyldihydro-γ-lumicolchicine with Sodium Borohydride.—A suspension of demethyldihydro-γ-lumicolchicine (100 mg.) in methanol (3 c.c.) was treated with a solution of sodium borohydride (30 mg.) in water (1 c.c.). After standing overnight, the resulting solution was worked up, as described above for the β-isomer, to give the glycol as a colourless glass.

Periodate Oxidation of the Glycol from Demethyldihydro-γ-lumicolchicine.—A solution of the glycol in methanol (1 c.c.) was treated with a solution of sodium metaperiodate (55 mg.) in water (2 c.c.). After 36 hr., the dialdehyde (X) was isolated as its *bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 144° depressed on admixture with the analogous compound of the β-series (Found: C, 52·9; H, 4·3; N, 16·6%). Light absorption in EtOH: $\lambda_{max.}$ 356 mμ.

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Perfluoroalkyl Derivatives of Sulphur. Part III. Some Reactions of Trifluoromethanethiol, and Spectroscopic Properties of the* >C:S *Group.*

By R. N. Haszeldine and J. M. Kidd.

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Trifluoromethanethiol is converted by anhydrous ammonia into trifluoromethyl fluorodithioformate and bistrifluoromethyl trithiocarbonate with intermediate formation of thiocarbonyl fluoride. Attempts to prepare the last compound are described. Its chloro-analogue yields dichlorodifluoromethane when treated with antimony trifluorodichloride, and carbonyl sulphide when hydrolysed. Other syntheses of trifluoromethyl fluorodithioformate and bistrifluoromethyl trithiocarbonate are given. Aqueous hydrolysis of trifluoromethanethiol yields thiocarbonyl fluoride and thence carbonyl sulphide. The hydrolysis of heptafluoropropanethiol, synthesised from bis(heptafluoropropyl) disulphide *via* bis(heptafluoropropylthio)mercury, is more complex, and is considered in connection with the hydrolysis of the disulphide.

The infrared spectra of compounds containing the >C:S group are considered and assignments are made for this group in various environments.

A convenient synthesis of trifluoromethanethiol from carbon disulphide was described earlier (*J.*, 1953, 3219), where it was shown that the thiol is stable *in vacuo* but decomposed by dilute aqueous sodium hydroxide with complete liberation of fluorine as fluoride and formation of carbonate and sulphide; no sulphur was formed. Further studies on the breakdown of trifluoromethanethiol under various conditions are now reported.

In ionising solvents or in presence of an acceptor for hydrogen fluoride, decomposition of trifluoromethanethiol occurs as follows: $CF_3{\cdot}SH \longrightarrow CSF_2 + HF$, and the thiocarbonyl fluoride often shows further reactions. Analytically pure thiocarbonyl fluoride has not been isolated, but its formation can be inferred from a series of related experiments.

Anhydrous ammonia reacts with trifluoromethanethiol to give, as volatile products, carbonyl sulphide, silicon tetrafluoride, and small amounts of a compound believed to be thiocarbonyl fluoride. The formation of carbonyl sulphide and silicon tetrafluoride, and the further etching of glass vessels when the mixture containing the probable thiocarbonyl fluoride is kept, together with a decrease in concentration of the last compound, show that it reacts with glass

$$2CSF_2 + SiO_2 \longrightarrow SiF_4 + 2COS$$

cf. $$2COF_2 + SiO_2 \longrightarrow SiF_4 + 2CO_2$$

The major products from the reaction with ammonia are a yellow liquid (b. p. 43°) of formula $C_2S_2F_4$, a red liquid (b. p. 110°) of formula $C_3S_3F_6$, and small amounts of a yellow solid, together with ammonium fluoride. The yellow liquid is trifluoromethyl fluorodithioformate (I) and the red liquid is bistrifluoromethyl trithiocarbonate (II). The yellow solid is possibly (III), produced by reaction of (I) with ammonia.

$CF_3{\cdot}S{\cdot}CSF$	$(CF_3{\cdot}S)_2CS$	$CF_3{\cdot}S{\cdot}CS{\cdot}NH_2$
(I)	(II)	(III)

Photochemical reaction of (I) with chlorine yields chlorotrifluoromethane, thus showing the presence of a CF_3 group, and the formation of a small amount of trifluoromethanethiol by reaction with water indicates a CF_3S group. Hydrolysis is slow at room temperature but rapid and complete at 75°. The aqueous solution then contains most of the fluoride

* Part II, *J.*, 1955, 2901.

and 13% of the sulphide, and carbonyl sulphide, carbon dioxide, and a small amount of trifluoromethanethiol are volatile products :

$$CF_3{\cdot}S{\cdot}CSF + 2H_2O \longrightarrow CF_3{\cdot}SH + (HO)_2CS + HF$$

$$\downarrow H_2O \qquad \downarrow$$

$$COS + 3HF \qquad COS + H_2O$$

$$\downarrow \qquad \downarrow$$

$$CO_2, H_2S \qquad CO_2, H_2S$$

Bistrifluoromethyl trithiocarbonate (II) similarly yields carbonyl sulphide when treated with water [(II) $\longrightarrow 2CF_3{\cdot}SH + (HO)_2CS \longrightarrow$ etc.]. The trithiocarbonate was synthesised by two routes :

$$2Hg(S{\cdot}CF_3)_2 + CSCl_2 \longrightarrow (CF_3{\cdot}S)_2CS + 2CF_3{\cdot}S{\cdot}HgCl$$

and

$$CF_3{\cdot}S{\cdot}CSF + Hg(S{\cdot}CF_3)_2 \longrightarrow (CF_3{\cdot}S)_2CS + CF_3{\cdot}S{\cdot}HgF$$

These provide proof of structure and establish the relationship between (I) and (II).

Trifluoromethyl fluorodithioformate is clearly formed *via* intermediate formation of thiocarbonyl fluoride :

$$CF_3{\cdot}SH \xrightarrow{NH_3} CSF_2 + HF$$

$$CF_3{\cdot}SH + CSF_2 \xrightarrow{NH_3} CF_3{\cdot}S{\cdot}CSF + HF$$

and bistrifluoromethyl trithiocarbonate by the further reaction

$$CF_3{\cdot}S{\cdot}CSF + CF_3{\cdot}SH \xrightarrow{NH_3} (CF_3{\cdot}S)_2CS + HF$$

Ammonia is essential to these reactions by acting as acceptor for hydrogen fluoride, since trifluoromethanethiol fails to yield bistrifluoromethyl trithiocarbonate when heated with thiocarbonyl chloride, or when treated with trifluoromethyl fluorodithioformate alone or in sulphur dioxide solution.

Attempts were made to synthesise thiocarbonyl fluoride, since, although Ruff is reported to have prepared this compound, it was shown (*J.*, 1953, 3219) that the compound obtained was actually thionyl fluoride. Reaction of thiocarbonyl chloride with zinc fluoride or antimony trifluoride failed to yield thiocarbonyl fluoride. At higher temperatures dichlorodifluoromethane was formed by replacement of sulphur by fluorine ($CSCl_2 \longrightarrow CF_2Cl_2$), and by decomposition of thiocarbonyl chloride ($2CSCl_2 \longrightarrow CS_2 + CCl_4$) followed by replacement of chlorine by fluorine in the carbon tetrachloride so produced. These reactions also explain the formation of trichlorofluoromethane and dichlorodifluoromethane during unsuccessful attempts to prepare bistrifluoromethyl sulphide from its chloro-analogue (Truce, Birum, and McBee, *J. Amer. Chem. Soc.*, 1952, **74**, 3594) :

$$(CCl_3)_2S \xrightarrow{SbF_3} CCl_4 + CSCl_2$$

$$\downarrow \qquad \downarrow$$

$$CFCl_3, CF_2Cl_2 \qquad CF_2Cl_2$$

Bistrichloromethyl sulphide is thermally unstable (Feichtinger and Moos, *Ber.*, 1948, **81**, 371) in sharp contrast to bistrifluoromethyl sulphide (*J.*, 1952, 2198). The chloro-compound differs also in its ready and complete breakdown to chloride, sulphide, and carbonate in presence of aqueous base, whereas bistrifluoromethyl sulphide is stable (*J.*, 1952, 2198); the fluoro-compound is cleaved by alcoholic potassium hydroxide at higher temperatures, however, to give a mixture of fluoroform, fluoride, sulphide, and carbonate :

$$CF_3{\cdot}S{\cdot}CF_3 \longrightarrow CF_3H + CF_3{\cdot}SOH \longrightarrow F^-, S^{--}, CO_3^{--}$$

Pyrolysis of bis(trifluoromethylthio)mercury also gave material containing thiocarbonyl fluoride :

$$Hg(S{\cdot}CF_3)_2 \longrightarrow HgF_2 + 2CSF_2$$

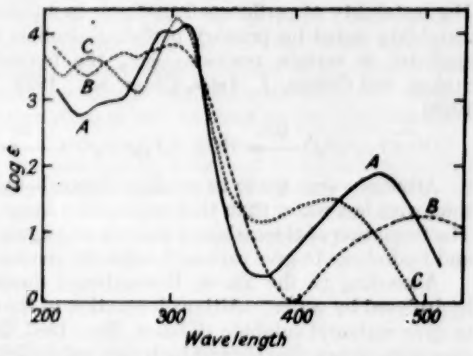
but attack of the last compound on the glass vessel again prevented its isolation pure. Pyrolysis of bistrifluoromethyl disulphide yielded carbon disulphide, carbon tetrafluoride, and bistrifluoromethyl sulphide, but only small amounts of thiocarbonyl fluoride.

The reaction of trifluoromethanethiol with anhydrous sodium fluoride gave a relatively high concentration of the compound believed to be thiocarbonyl fluoride:

$$CF_3{\cdot}SH + NaF \longrightarrow CSF_2 + NaHF_2$$

but carbonyl sulphide and silicon tetrafluoride formation again prevented complete identification. Trifluoromethyl fluorodithioformate (I) was also formed by reaction of the thiocarbonyl fluoride with trifluoromethanethiol, and sodium fluoride acts like ammonia in this respect, though less efficiently.

Ultraviolet spectra in light petroleum.
. . . . Dimethyl trithiocarbonate.
– – – – Bistrifluoromethyl trithiocarbonate.
——— Ethylene trithiocarbonate.



The general similarity of the ultraviolet spectra of bistrifluoromethyl, dimethyl, and ethylene trithiocarbonates is brought out by the diagram better than by the precise values given in the annexed Table, which includes data for diethyl trithiocarbonate and trifluoromethyl fluorodithioformate.

Compound	Solvent	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$
$CF_3{\cdot}S{\cdot}CSF$	Light petroleum	393	22	343	9
		269	7400	240	6150
	Vapour	393	16	330·5	2·48
		330	2·54	328·5	2·44
		327	2·58	325·5	2·48
		324	2·65	332·5	2·60
		322·5	2·80	322	2·73
		263	4100	235	680
$(CF_3{\cdot}S)_2CS$	Light petroleum	496	16	396	1
		299	6400	267	4300
		259	4900	230	2250
	Vapour	293	4150	282	3790
		277	3900	262	3120
		254	3790	251	3780
		248	3800	247	3780
		246	3790	226	1900
$(CH_3{\cdot}S)_2CS$ [1]	*cyclo*Hexane	430	28	—	—
		302	16,900	—	—
		238	3780	—	—
$(C_2H_5{\cdot}S)_2CS$ [1]	,,	432	36	—	—
		305	19,400	—	—
		238	4000	—	—
$CH_2{\cdot}S$ / $CH_2{\cdot}S$ > CS [2]	Light petroleum	460	69	298	10,300
		311	12,500	227	335
		292	10,600	—	—

[1] Challenger, Mason, Holdsworth, and Emmett, *J.*, 1953, 292. [2] Challenger *et al.* report maxima at 458, 311·5, and 293 mμ (ε 72, 14,780, and 12,640 respectively) for a solution in *cyclo*hexane.

The results of the aqueous hydrolysis of trifluoromethanethiol can now be interpreted. Reaction with a large excess of water at 0° produces a small amount of a yellow liquid shown

to be trifluoromethyl fluorodithioformate (I). This slowly disappears when kept in contact with water, and the aqueous solution then contains all the fluorine as fluoride, and carbonyl sulphide is the major volatile product. Since carbonyl sulphide is slowly hydrolysed to carbon dioxide and hydrogen sulphide, small amounts of these compounds are also formed. The formation of carbonyl sulphide and trifluoromethyl fluorodithioformate is again evidence for intermediate formation of thiocarbonyl fluoride :

$$CF_3{\cdot}SH \xrightarrow{H_2O} HF + CSF_2 \longrightarrow COS + 2HF$$
$$\downarrow CF_3{\cdot}SH$$
$$CF_3{\cdot}S{\cdot}CSF$$

The instability of perfluoroalkanethiols in aqueous media is in agreement with the similar instability noted for primary perfluoro-alcohols when such compounds are plausible intermediates in certain reactions, *e.g.*, the hydrolysis of perfluoro-lactones (Hauptschein, Stokes, and Grosse, *J. Amer. Chem. Soc.*, 1952, **74**, 1974; Haszeldine, *Nature*, 1951, **168**, 1028) :

$$\overbrace{OC{\cdot}[CF_2]_3{\cdot}CF_2O} \xrightarrow{H_2O} HO_2C{\cdot}[CF_2]_3{\cdot}CF_2{\cdot}OH \xrightarrow{-HF} HO_2C{\cdot}[CF_2]_3{\cdot}COF \xrightarrow{H_2O} HO_2C{\cdot}[CF_2]_3{\cdot}CO_2H$$

Attempts were made to produce thiocarbonyl fluoride by reaction of trifluoromethanethiol with less water than that required to cause complete hydrolysis to carbonyl sulphide. The formation of thiocarbonyl fluoride was again very probable, but its reaction with glass, and hydrolysis to give carbonyl sulphide, rendered its purification impossible.

According to the above, thiocarbonyl fluoride should yield carbonyl sulphide when hydrolysed by water. Although reaction of thiocarbonyl chloride with ethanol is reported to give carbonyl sulphide (Klason, *Ber.*, 1887, **20**, 2384), its aqueous hydrolysis is said to give only carbon dioxide and hydrogen sulphide (Bergreen, *Ber.*, 1888, **21**, 337), not carbonyl sulphide. Böhme (*ibid.*, 1941, **74**, *B*, 248) studied the rate of hydrolysis of thiocarbonyl chloride with water at room temperature, but did not report any gaseous products. Re-examination has now shown that thiocarbonyl chloride reacts only slowly with water at room temperature, but that carbonyl sulphide, together with its hydrolysis products carbon dioxide and hydrogen sulphide, is formed at 100°; this is completely in accord with the reactions postulated for thiocarbonyl fluoride.

Thiocarbonyl fluoride could probably be prepared in high yield by pyrolysis of trifluoromethanethiol in a platinum tube. At low temperatures and in absence of moisture it will probably be stable to glass, like carbonyl fluoride.

Studies on the hydrolysis of heptafluoro-*n*-propanethiol were made in attempt to throw further light on the proposed mechanism for perfluoroalkanethiol hydrolysis. The thiol was prepared by a method analogous to that used for trifluoromethanethiol :

$$C_3F_7I \xrightarrow{S} (C_3F_7)_2S_3 \xrightarrow{Hg,\ h\nu} (C_3F_7{\cdot}S)_2Hg \xrightarrow{HCl} C_3F_7{\cdot}SH + HgCl_2$$

The preparation of the disulphide by the general method outlined earlier (*Nature*, 1950, **166**, 225; *J.*, 1952, 2198) offered no difficulty, but formation of the mercurial was more troublesome. At an optimum reaction temperature of 75° a crystalline solid appears within a few minutes of exposure to ultraviolet light, but reaction is then inhibited, and prolonged irradiation only decomposes the yellow solid. Bis(heptafluoro-*n*-propylthio)mercury was isolated as a thick oil, and when treated with anhydrous hydrogen chloride gave heptafluoro-*n*-propanethiol, b. p. 23·7°; the overall yield from the disulphide was low. The infrared spectrum of the thiol shows a sharp band at 3·82 μ assigned to the S–H stretching vibration (cf. trifluoromethanethiol 3·84 μ).

The following reaction scheme was expected for the aqueous hydrolysis of heptafluoro-*n*-propanethiol :

$$C_3F_6{\cdot}CF_2{\cdot}SH \xrightarrow{H_2O} HF + C_3F_6{\cdot}CSF \xrightarrow{H_2O} C_3F_6{\cdot}CS{\cdot}OH + HF$$

with possibly further reaction of the thio-acid to give pentafluoropropionic acid. Two atoms of fluorine should thus be liberated as fluoride, with a negligible amount of

sulphide. The thiol is immiscible with, and only very slowly attacked by, water at room temperature, but at 100°, 2·0—2·3 atom-equiv. of fluorine are liberated as fluoride, with negligible formation of sulphide, in reasonable agreement with prediction. The immiscible liquid went deep yellow before it slowly decomposed, and this is attributed to intermediate formation of (IV) and/or (V) :

$$C_3F_7\cdot SH \longrightarrow HF + \underset{\text{(IV)}}{C_3F_5\cdot CSF} \xrightarrow{C_3F_7\cdot SH} \underset{\text{(V)}}{C_3F_5\cdot CS\cdot S\cdot C_3F_7}$$

Aqueous alkaline hydrolysis of heptafluoro-*n*-propanethiol is more complicated than the expected formation of pentafluoropropionic acid with liberation of two atoms of fluorine as fluoride and one atom of sulphur as sulphide per molecule of thiol. A deep-red solution is produced by reaction with aqueous base, and 2·8—3·0 atom-equiv. of fluoride and 0·84—1·00 of sulphide are formed at temperatures ranging from 20° to 140°. The sulphide formation is as expected, but an extra atom of fluorine is liberated. This is not caused by formation of tetrafluoroethylene from sodium pentafluoropropionate ($C_2F_5\cdot CO_2Na \longrightarrow C_2F_4 + CO_2 + NaF$; cf. *J.*, 1952, 4259), since no volatile products were detected. Heptafluoropropanethiol thus loses an extra fluorine atom as well as those on the α-carbon atom in presence of aqueous base.

The above result is in agreement with the alkaline hydrolysis of bisheptafluoropropyl disulphide, which reacts at room temperature, more rapidly when heated, to give a red solution containing 5 equiv. of fluoride and 1·6 of sulphide. This is consistent with S–S bond fission as postulated earlier (Part II, *loc. cit.*) for bistrifluoromethyl disulphide :

$$C_3F_7\cdot S\cdot S\cdot C_3F_7 \xrightarrow{OH^-} C_3F_7\cdot SH + C_3F_7\cdot S\cdot OH$$

$$C_3F_7\cdot SH \xrightarrow{OH^-} 3F^-, S^{--}$$

$$C_3F_7\cdot S\cdot OH \xrightarrow{OH^-} \tfrac{1}{2}C_3F_7\cdot SH + \tfrac{1}{2}C_3F_7\cdot SO_3H$$

$$\tfrac{1}{2}C_3F_7\cdot SH \xrightarrow{OH^-} 1\tfrac{1}{2}F^-, \tfrac{1}{2}S^{--}$$

$$\tfrac{1}{2}C_3F_7\cdot SO_3H \xrightarrow{OH^-} \text{no fluoride}$$

The heptafluoropropanethiol yields 3 equiv. of fluoride and one of sulphide, and the sulphenic acid disproportionates as demonstrated for trifluoromethanesulphenic acid (Part II, *loc. cit.*) to give the thiol and the sulphinic acid. The last compound, like trifluoromethanesulphinic acid, does not liberate fluoride with aqueous base, though it would probably give heptafluoropropane at higher temperatures (cf. $CF_3\cdot SO_2H \xrightarrow{55°} CF_3\cdot SO_2Na \xrightarrow{95°} CHF_3$). By the above scheme 4·5 equiv. of fluoride and 1·5 of sulphide are expected; the experimental figure for sulphide agrees well with this, but that for fluoride is slightly high, indicating an alternative or side-reaction. This could be C–S fission instead of S–S fission :

$$C_3F_7\cdot S\cdot S\cdot C_3F_7 \xrightarrow{OH^-} C_3F_7\cdot OH + C_3F_7\cdot S\cdot SH$$

$$C_3F_7\cdot OH \xrightarrow{OH^-} C_3F_5\cdot CO_2H + 2F^-$$

$$C_3F_7\cdot S\cdot SH \xrightarrow{OH^-} C_3F_7\cdot SH + S$$

$$S \xrightarrow{OH^-} 3F^-, S^{--}$$

By this route 5 equiv. of fluoride and 2 of sulphide (including polysulphides) would be formed. Assessment of its importance is not yet possible.

Infrared Spectra of Compounds containing the >C:S *Group.*—Very few studies have been reported on the spectroscopic characteristics of the >C:S group. The strong band at 6·57 μ for carbon disulphide has been assigned to the C:S stretching vibration (Herzberg, "Infra-red and Raman Spectra of Polyatomic Molecules," van Nostrand, 1945, p. 276), and the corresponding band in carbonyl sulphide was considered to be at 11·64 μ (Bailey and Cassie, *Proc. Roy. Soc.*, 1932, *A*, **135**, 375). These assignments are of little value in deciding where the C:S vibration will appear in compounds such as dithioformates or

trithiocarbonates. The following argument leads to a fairly certain assignment for the C:S vibration in such compounds, however.

Dialkyl carbonates, $(RO)_2CO$, absorb strongly at *ca.* 5·70 μ and this is assigned to the C:O stretching vibration in such compounds (unpublished results). The C:O stretching vibration in carbonyl chloride is at 5·45 μ (doublet at 5·43, 5·47 μ), so that the groups RO and Cl have much the same effect on the C:O vibration, with the more powerful inductive effect of the chlorine atom causing a shift to shorter wavelength. To a first approximation, therefore, the C:S stretching vibration in thiocarbonyl chloride should lie at longer wavelength than the C:O vibration in carbonyl chloride, and should be not far removed from the C:S vibration in a trithiocarbonate $(RS)_2CS$. The infrared spectrum of thiocarbonyl chloride (C.S. No. 277) * shows a powerful band at 8·80 μ which is assigned to the C:S stretching vibration. The doublet at 12·33, 12·60 μ is assigned to the C–Cl stretching vibrations; that at 5·44, 5·47 μ cannot be the C:S stretching vibration, since it is at the same position as the C:O vibration in carbonyl chloride. It is noteworthy that similar doublets occur in the spectra of carbon disulphide (4·57, 4·60 μ) and carbonyl sulphide (C.S. No. 278; 4·84, 4·87 μ). The strong doublet in the spectrum of carbonyl sulphide at 11·55, 11·80 μ is presumably the 11·64 μ band noted by the earlier workers, and their band at 9·52 μ is similarly resolved into a doublet at 9·47, 9·65 μ.

The infrared spectrum of ethylene trithiocarbonate (C.S. No. 279) shows a very powerful band at 9·27 μ and this is assigned to the C:S stretching vibration. It is at the expected position relative to thiocarbonyl chloride. Introduction of fluorine into the molecule, as with bistrifluoromethyl trithiocarbonate, should cause a shift of the C:S vibration to shorter wavelength just as the C:O, NO_2, or SO_2 stretching vibrations are shifted to shorter wavelength by the increased inductive effect on replacement of alkyl by perfluoroalkyl (Haszeldine, *Nature*, **1951**, **168**, 1028; *J.*, **1953**, 2525; Haszeldine and Kidd, Part II, *loc. cit.*). The infrared spectrum of bistrifluoromethyl trithiocarbonate (C.S. No. 280) is simple, with a strong doublet at 8·36, 8·45 μ and a strong band at 9·09 μ. The 9·09 μ absorption is assigned to the C:S vibration, and the 8·36, 8·45 μ doublet to the C–F stretching vibrations which usually appear in this region; it should be noted that there are no bands of even medium intensity between 2 and 8 μ, so the C:S vibration cannot appear in this region. Finally, trifluoromethyl fluorodithioformate shows a spectrum (C.S. No. 281) with powerful absorption at 8·10, 8·45, and 8·89 μ. Replacement of a CF_3·S group in bistrifluoromethyl trithiocarbonate by a fluorine atom should cause a shift of the C:S vibration to shorter wavelength, and the 8·89 μ band is therefore assigned to this vibration, and the 8·10 and 8·45 μ bands to the C–F stretching vibrations.

The position of the C:S vibration for other compounds can now be predicted, as shown in the annexed Table.

Compound	R = alkyl	R = perfluoroalkyl	Compound	R = alkyl	R = perfluoroalkyl
$(RO)_2C:S$	8·95—9·30	8·75—9·10	RS·CSF	8·9—9·3	8·85—9·05
$(RS)_2C:S$	9·25—9·50	9·05—9·20	RS·CSCl	9·1—9·4	9·1—9·3
$R_2C:S$	9·3—9·7	9·1—9·5			

Experimental

See earlier papers for preparation of starting materials and techniques used.

Reaction of Trifluoromethanethiol with Ammonia.—In a typical experiment, trifluoromethanethiol (0·9465 g., 0·00937 mole) and anhydrous ammonia (0·1605 g., 0·00944 mole) in a 30-ml. sealed tube were allowed to warm from −80° to room temperature. During this time a red compound was formed and a white solid was deposited. Fractionation of the volatile products by bulb-to-bulb distillation *in vacuo* gave (i) a small volatile fraction (0·0804 g.; *M*, 72), (ii) *trifluoromethyl fluorodithioformate* (0·3076 g., 40%), a yellow liquid, b. p. 42·9°/762 mm. (isoteniscope) (Found: F, 45·9; S, 39·2%; *M*, 164. $C_2F_4S_2$ requires F, 46·3; S, 39·0%; *M*, 164), and (iii) *bistrifluoromethyl trithiocarbonate* (0·2045 g., 10%), a red liquid, b. p. 110° (micro) (Found: F, 45·7; S, 38·3%; *M*, 248. $C_3F_6S_3$ requires F, 46·3; S, 39·0%; *M*, 246). The first

* Spectra thus marked have been deposited with the Society. Photocopies may be obtained, price 3s. 0d. each, on application to the General Secretary, quoting the C.S. No.

fraction was treated with anhydrous hydrogen chloride to remove any ammonia, then refractionated; infrared spectroscopic examination showed it to contain trifluoromethanethiol, carbonyl sulphide, silicon tetrafluoride, and probably thiocarbonyl fluoride.

The solid produced in the reaction was extracted with water to remove ammonium fluoride, leaving a yellow solid containing fluorine and nitrogen.

Reaction of Trifluoromethyl Fluorodithioformate with Chlorine.—Chlorine (0·274 g.) and the thioformate (0·1029 g.) in a silica tube were exposed to ultraviolet light (2 weeks). A yellow crystalline solid formed in the early stages slowly disappeared as irradiation continued. Distillation gave chlorotrifluoromethane (0·0351 g., 53%) (*M*, 105), identified spectroscopically, unchanged chlorine (0·192 g., 70%), and a mixture (0·131 g.) of unchanged trifluoromethyl fluorodithioformate and sulphur chlorides.

Synthesis of Bistrifluoromethyl Trithiocarbonate.—(a) *From trifluoromethyl fluorodithioformate.* The dithioformate (0·1638 g.) and bis(trifluoromethylthio)mercury (0·493 g.) underwent no reaction at room temperature in a sealed tube. After 24 hours' heating at 70° a red liquid had formed and appreciable etching was apparent. Distillation gave bistrifluoromethyl trithiocarbonate (0·0852 g., 34%) (Found: *M*, 244. Calc. for $C_3F_6S_3$: *M*, 246), identified spectroscopically, and two smaller unidentified fractions. Ether extraction of the solid reaction products gave unchanged mercurial (0·256 g., 52%), m. p. 36°.

(b) *From thiocarbonyl chloride.* Bis(trifluoromethylthio)mercury (0·8775 g.) and thiocarbonyl chloride (0·1819 g.) in a 30-ml. sealed tube reacted only when heated at 50° (24 hr.) to give bistrifluoromethyl trithiocarbonate (0·2362 g., 61% based on thiocarbonyl chloride) (Found: *M*, 245), identified spectroscopically, and unchanged thiocarbonyl chloride. The colourless, needle-like crystals also produced during the reaction were extracted with ether to give trifluoromethylthiomercuric chloride (0·7107 g., 97%), m. p. 124—126° (Found: Cl, 11·6. Calc. for $CClF_3SHg$: Cl, 10·5%), slightly contaminated by mercuric chloride from which it could not be separated by differential solvent extraction. The mercurichloride has the typical pungent odour associated with perfluoroalkylmercury compounds.

(c) *Attempted syntheses.* Trifluoromethanethiol (0·0982 g.) and trifluoromethyl fluorodithioformate (0·1080 g.) were unchanged after being kept at 20° (2 days). Addition of liquid sulphur dioxide to act as ionising solvent failed to cause reaction after 3 days.

Thiocarbonyl chloride (0·1268 g.) and trifluoromethanethiol (0·2863 g.) showed no signs of reaction in a 10-ml. sealed tube at 20°, but after 4 days' heating at 75° considerable etching and a faint red coloration could be detected. Distillation gave only unchanged thiocarbonyl chloride (0·1075 g.) and breakdown products, and not more than a small amount of bistrifluoromethyl trithiocarbonate.

Hydrolysis of Trifluoromethyl Fluorodithioformate.—The dithioformate (0·0884 g.) slowly reacted with water (2·5 ml.) in a 10-ml. sealed tube; after 12 hours' heating at 75° no yellow liquid remained. Distillation gave a volatile product shown by infrared spectroscopic examination to contain mainly carbonyl sulphide with small amounts of carbon dioxide and trifluoromethanethiol. The gaseous product was completely decomposed by 15% aqueous sodium hydroxide, and the fluoride and sulphide so formed were estimated (Found: F^-, 2·5; S^{--}, 86% based on trifluoromethyl fluorodithioformate). The fluoride and sulphide in the aqueous solution from the original hydrolysis were also estimated (Found: F^-, 98; S^{--}, 13%).

Hydrolysis of Bistrifluoromethyl Trithiocarbonate.—The thiocarbonate (0·0825 g.) and water (2 ml.) showed no reaction in a 10-ml. sealed tube, but reacted completely at 80° (18 hr.). The volatile product was shown by infrared spectroscopic examination to be mainly carbonyl sulphide; it was completely absorbed by 15% aqueous sodium hydroxide (Found: F^-, 2; S^{--}, 74%). The aqueous solution from the hydrolysis contained F^-, 96; and S^{--}, 23%.

Hydrolysis of Thiocarbonyl Chloride.—The chloro-compound (0·2320 g.) and water (4 ml.) in a 30-ml. Pyrex tube underwent little reaction at 25° (12 hr.), but at 100° (1 hr.) almost complete reaction occurred to give unchanged thiocarbonyl chloride (0·0341 g., 14%) (Found: *M*, 113. Calc. for $CSCl_2$: *M*, 115) and slightly impure carbonyl sulphide (0·112 g.), identified by means of its infrared spectrum. Analysis of the gaseous reaction products other than thiocarbonyl chloride gave S^{--}, 81; Cl^-, 2%, based on the thiocarbonyl chloride taken. Analysis of the aqueous solution showed it to contain S^{--}, 3; Cl^-, 84%, based on the thiocarbonyl chloride taken; with allowance for that recovered unchanged (14%), the weight balance for chloride is 100%, and for sulphide 98%.

Carbonyl sulphide (Found: *M*, 60. Calc. for COS: *M*, 60) was prepared as reference compound from ammonium thiocarbamate (Stock and Kuss, *Ber.*, 1917, **50**, 159). The vapour pressures at various temperatures agreed with those reported by Stock and Kuss.

Attempted Preparation of Thiocarbonyl Fluoride from Thiocarbonyl Chloride.—Thiocarbonyl chloride, b. p. 74·2—74·4° (Found : *M*, 115. Calc. for CCl_2S : *M*, 115) was dried over phosphoric anhydride. (*a*) Anhydrous zinc fluoride (10 g.) and thiocarbonyl chloride (3·0 g.), heated at 130° (12 hr.) in a 100-ml. autoclave in absence of air, underwent no reaction.

(*b*) Freshly-sublimed antimony trifluoride and thiocarbonyl chloride failed to react when heated at 90° (12 hr.) in an autoclave.

(*c*) Antimony trifluoride (35 g.) and chlorine (2·6 g.) were heated in an autoclave to form the quinquevalent salt. Thiocarbonyl chloride (3·6 g.) was then added, and the mixture heated at 230° (4 hr.) to give dichlorodifluoromethane (1·12 g., 30%), b. p. −29·9° (Found : *M*, 121. Calc. for CCl_2F_2 : *M*, 121), identified by means of its infrared spectrum, and a mixture (0·190 g.) containing dichlorodifluoromethane and chlorotrifluoromethane. Similar products were formed at lower temperatures.

Pyrolysis of Bis(trifluoromethylthio)mercury.—The mercurial (0·976 g.), heated at 220° (48 hr.) in a silica tube, gave volatile products containing carbonyl sulphide, a small amount of bistrifluoromethyl sulphide, carbon dioxide, silicon tetrafluoride, and a material believed to be thiocarbonyl fluoride.

Pyrolysis of Bistrifluoromethyl Disulphide.—Small amounts of thiocarbonyl fluoride were produced when bistrifluoromethyl disulphide was heated at 320° (24 hr.) in a steel autoclave. The main products were (*a*) carbon disulphide, b. p. 45° (Found : *M*, 77. Calc. for CS_2 : *M*, 76), (*b*) a mixture of unchanged bistrifluoromethyl disulphide and carbon disulphide, (*c*) carbon tetrafluoride (Found : *M*, 88. Calc. for CF_4 : *M*, 88), and (*d*) bistrifluoromethyl sulphide (Found : *M*, 169. Calc. for C_2F_6S : *M*, 170). The products were identified spectroscopically.

Hydrolysis of Trifluoromethanethiol.—(a) *With an excess of water.* The thiol (0·131 g.) was sealed with water (2 ml.) in a 10-ml. Pyrex tube, and allowed to warm to room temperature. As soon as the ice was melted fumes were evolved and a small amount of a yellow immiscible liquid was formed; the yellow liquid disappeared after 12 hr. The aqueous solution was made alkaline and the fluoride and sulphide present were determined (Found : F^-, 98% of total fluorine; S^{--}, 7% of total sulphur). The volatile reaction products (0·079 g.) of the aqueous hydrolysis were carbonyl sulphide and a very small amount of unchanged trifluoromethanethiol as shown by an infrared spectrum of the mixture. The mixture was completely decomposed by 15% aqueous sodium hydroxide (Found : F^-, 1% of toal fluorine; S^{--}, 90% of total sulphur).

In another experiment trifluoromethanethiol (0·141 g.) and water (2·5 ml.) were allowed to react as above to give the yellow liquid which was then transferred to a vacuum apparatus for the manipulation of gases. After purification the yellow liquid (0·032 g.) was shown by molecular-weight determination (Found : *M*, 164) and infrared spectroscopic examination to be trifluoromethyl fluorodithiocarbonate.

(b) *With small amounts of water.* The thiol (0·1017 g., 0·00099 mole) and water (0·0122 g., 0·00068 mole) were kept in a 30-ml. Pyrex tube at room temperature (12 hr.) to give unchanged trifluoromethanethiol, small amounts of carbonyl sulphide, silicon tetrafluoride, and a substance believed to be thiocarbonyl fluoride. The products were identified by means of their infrared spectra. The amount of the material believed to be thiocarbonyl fluoride decreased, and finally disappeared, when it was treated with successive small quantities of water, and carbonyl sulphide and silicon tetrafluoride were produced and identified spectroscopically. Similar decomposition was detected in subsequent experiments when the thiocarbonyl fluoride fraction was heated in a glass vessel. Attempts to purify thiocarbonyl fluoride failed.

Reaction of Trifluoromethanethiol with Sodium Fluoride.—Anhydrous sodium fluoride (0·490 g.) in a 30-ml. Pyrex tube was heated *in vacuo* to remove last traces of moisture before addition of trifluoromethanethiol (0·1061 g.). After 2 days at room temperature, distillation gave trifluoromethyl fluorodithioformate (0·0151 g.) (Found : *M*, 160. Calc. for $C_2S_2F_4$: *M*, 164), identified by means of its infrared spectrum, and a more volatile fraction (0·0470 g.) shown by infrared spectroscopic examination to contain trifluoromethanethiol, carbonyl sulphide, silicon tetrafluoride, and a comparatively large amount of thiocarbonyl fluoride.

A similar reaction at 55° (6 hr.) failed to yield thiocarbonyl fluoride, and the amounts of carbonyl sulphide and silicon tetrafluoride had increased, thus revealing the thermal instability of thiocarbonyl fluoride.

Reaction of Bistrifluoromethyl Sulphide with Alcoholic Potassium Hydroxide.—The sulphide was recovered unchanged after treatment with an excess of 10% alcoholic potassium hydroxide at 70—75° for 24 hr. Bistrifluoromethyl sulphide (0·2189 g.) and 20% alcoholic potassium hydroxide (10 ml.), heated at 100° (48 hr.), gave unchanged bistrifluoromethyl sulphide (5%) and fluoroform (25%) (Found : *M*, 70. Calc. for CHF_3 : *M*, 70), identified by means of their

infrared spectra. The alcoholic solution was diluted with water and the fluoride in it (0·0880 g., 60%) was determined by distillation to give fluorosilicic acid and titration with thorium nitrate in the usual way.

*Bis(heptafluoro-*n*-propyl) Disulphide.*—Heptafluoroiodopropane was prepared in 86% yield by reaction of silver heptafluorobutyrate (150 g., 0·467 mole) and dry iodine (240 g., 0·945 mole) as described earlier (*J.*, 1951, 584; 1952, 4259).

Little reaction occurred between heptafluoroiodopropane and sulphur in a steel autoclave at temperatures up to 350°; at 400° there was 50% reaction, and at 450° no heptafluoroiodopropane remained unchanged. In a typical experiment, sulphur (60 g.) and heptafluoroiodopropane (86 g.) were heated (14 hr.) at 450° in a 300-ml. stainless-steel autoclave to give bis(heptafluoro-*n*-propyl) disulphide (21 g., 36%), b. p. 122°, and several fractions containing impure disulphide and small amounts of monosulphide and polysulphides. Hauptschein and Grosse (*J. Amer. Chem. Soc.*, 1951, **73**, 5461) used this general method as developed for trifluoroiodomethane and reported b. p. 122° for the disulphide.

Bis(heptafluoropropyl) disulphide has the following ultraviolet spectrum: $\lambda_{max.}$ 244, ε 875, $\lambda_{min.}$ 218, ε 385 in ethanol, and $\lambda_{max.}$ 242, ε 860, $\lambda_{min.}$ 218, ε 370 in light petroleum; this shows the expected shift to longer wavelength relative to bistrifluoromethyl disulphide (*J.*, 1952, 2549) ($\lambda_{max.}$ 236, ε 390 in light petroleum) on change of a CF_3 to a heavier C_3F_7 group. The infrared spectrum of bis(heptafluoropropyl) disulphide (C.S. No. 282) shows the typical carbon–fluorine stretching vibrations.

Heptafluoropropanethiol.—Reaction of bis(heptafluoropropyl) disulphide with mercury in a silica tube in ultraviolet light at room temperature was slow and any mercurials formed were decomposed to mercuric sulphide. A vigorously-shaken 30-ml. silica tube containing bis(heptafluoropropyl) disulphide (2·0 g.) and mercury (15 g.) was heated at 80° by means of an open framework heater designed so that ultraviolet light from a Hanovia S-250 arc could enter the tube. After 2 days' irradiation a black solid had been formed. The liquid and volatile products were removed by pumping to leave a viscous black mass in the tube which was extracted with ether; subsequent evaporation of the ether yielded a pale yellow viscous liquid with a very pungent odour. This is bis(heptafluoropropylthio)mercury.

A series of similar reactions at temperatures between 40° and 100° showed that the optimum temperature was 70—80°; above this temperature excessive decomposition occurred, and below it only small amounts of the mercurial were obtained. A large excess of mercury (80 moles per mole of disulphide) was also necessary. Formation of a yellow crystalline compound could be observed within a few minutes of exposure to light at 75°, but the reaction slowed rapidly and an irradiation time of 2 days was found convenient. Repeated experiments were thus necessary to obtain an appreciable quantity of the mercurial. The yield was *ca.* 10%.

Bis(heptafluoropropylthio)mercury (1·0 g.) was treated with anhydrous hydrogen chloride (0·2 g.) in a 30-ml. sealed tube to give (24 hr.) mercuric chloride and *heptafluoropropanethiol* (0·301 g.), b. p. 23·7°/759 mm. (isoteniscope) (Found: F, 65·0; S, 15·5%; *M*, 202. C_3HF_7S requires F, 65·8; S, 15·8%; *M*, 202).

Hydrolysis of Heptafluoropropanethiol.—(a) *With water.* The thiol (0·0720 g.) and water (2 ml.) showed but little reaction at 20° (3 days), but after 3 days at 55° and 12 hr. at 75° most of the thiol had disappeared. The temperature was raised to 100° (24 hr.), and only a small amount of yellow immiscible liquid remained. There were no volatile products. The aqueous solution was extracted with ether to remove any organic matter, then analysed for fluoride in the usual way. The fluoride was equivalent to 2·07 fluorine atoms per molecule of heptafluoropropanethiol taken; the sulphide was negligible.

In a second experiment heptafluoropropanethiol (0·0653 g.) and water (2 ml.) were heated at 100° (36 hr.). The fluoride liberated was equivalent to 2·3 fluorine atoms per molecule of the thiol, and negligible sulphide was formed.

(b) *With aqueous sodium hydroxide.* The thiol (0·1001 g.) was condensed into a tube containing 10% aqueous sodium hydroxide (2·5 ml.), and the tube was then sealed. As the aqueous solution began to melt the suspension of the thiol turned deep yellow then slowly disappeared (14 hr.) to give a deep red aqueous solution. There were no volatile products, and the aqueous solution contained fluoride equivalent to 2·8 fluorine atoms and sulphide equivalent to 0·84 sulphur atom per molecule of heptafluoropropanethiol.

A second experiment with the thiol (0·1209 g.) and 10% aqueous sodium hydroxide (4 ml.) at 75° (6 hr.) gave fluoride equivalent to 3·0 fluorine atoms and sulphide equivalent to 1·0 sulphur atom per molecule of thiol. A third experiment, at 130—140° (20 hr.), gave fluoride equivalent to 2·93 fluorine atoms.

Reaction of Bisheptafluoropropyl Disulphide with Aqueous Sodium Hydroxide.—The disulphide (0·2338 g.) and 20% aqueous sodium hydroxide (6 ml.) in a 30-ml. sealed tube reacted slowly at room temperature to give an orange aqueous layer. Only a small amount of immiscible liquid remained after 8 hr. at 85°, and the solution was deep red; there were no volatile products. The aqueous solution was extracted with ether then analysed for fluoride and sulphide (Found: F^- equivalent to 4·3 fluorine atoms, S^{--} equivalent to 1·0 sulphur atom per molecule of disulphide). A second experiment at 85° (4 days) gave F^- equivalent to 5·04 fluorine atoms, S^{--} equivalent to 1·6 sulphur atoms.

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University Chemical Laboratory, Cambridge. [*Received, May 24th*, 1955.]

Fluoro-olefins. Part III. Some Rearrangement Reactions of Polyhalogeno-olefins, and Routes to Butadienes.†*

By R. N. Haszeldine and J. E. Osborne.

[Reprint Order No. 6512.]

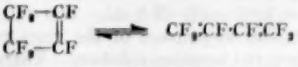
The equilibrium between polyhalogenobutadiene and polyhalogeno-*cyclo*butene obtains at high temperatures; use is made of this to synthesise perfluorobutadiene in high yield by reaction of perfluoro*cyclo*butene with hydrogen iodide to give $CHF_2{\cdot}CHF{\cdot}CHF{\cdot}CHF_2$ followed by chlorination and treatment with zinc and ethanol.

Thermal dimerisation of $CFCl{:}CFCl$ yields exclusively $CFCl_2{\cdot}CFCl{\cdot}CF{:}CFCl$, dechlorination of which gives $CFCl{:}CF{\cdot}CF{:}CFCl$. The diene is converted into 2 : 3-dichlorotetrafluoro*cyclo*butene when heated, and chlorination of the last compound gives 1 : 2 : 3 : 4-tetrachlorotetrafluoro*cyclo*butane; this cannot be obtained by cyclic dimerisation of 1 : 2-dichlorodifluoroethylene. Attempts to prepare perfluoro*cyclo*buta-1 : 3-diene were unsuccessful. Proofs of structure are given involving the preparation of $CFCl_2{\cdot}CFCl{\cdot}CO_2H$ and $(CFCl{\cdot}CO_2H)_2$.

Reaction schemes are considered for the open-chain dimerisation of polyhalogeno ethylenes and it is concluded that either a non-radical reaction, possibly involving a *cyclo*butane intermediate, or a radical-chain reaction can occur under suitable conditions. Predictions are made for $CF_2{:}CCl_2$, $CFCl{:}CCl_2$, $CF_2{:}CHCl$, $CHF{:}CCl_2$, and $CHCl{:}CCl_2$.

Syntheses of polyfluorobutadienes have been described (*J.*, 1952, 4423; 1953, 3371; 1954, 4026). The present communication describes certain rearrangements of polyfluoro-olefins which may be used to synthesise polyhalogeno-butadienes or -*cyclo*butanes.

Miller (in "Preparation, Properties, and Technology of Fluorine and Organic Fluoro-compounds," Slesser and Schramm, McGraw-Hill, New York, 1951; Prober and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 598) has shown that, when heated at 150—180°, hexafluorobutadiene is converted into hexafluoro*cyclo*butene and mixed dimers C_8F_{12} and trimers $C_{12}F_{18}$. We have now found that perfluoro*cyclo*butene can be isomerised by heat into perfluorobutadiene, *i.e.*,

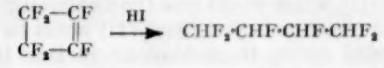


The equilibrium, with its attendant side-reactions, can also be attained from perfluorobutadiene. Perfluoro*cyclo*hexene does not react analogously; this illustrates the difference in stability between the 4- and 6-membered rings.

* Part II, *J.*, 1953, 3371.

† Presented in part at the Amer. Chem. Soc. Meeting, Minneapolis, 1955.

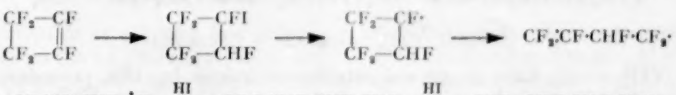
An interesting reaction occurs when perfluoro*cyclo*butene is heated with hydrogen iodide, since 1 : 1 : 2 : 3 : 4 : 4-hexafluorobutane is produced in excellent yield :

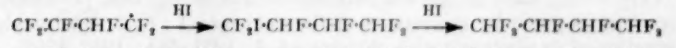


The hexafluorobutane boils at 64° and the marked increase in b. p. on replacement of fluorine by hydrogen is noteworthy (cf. *n*-C_4F_{10} b. p. −5°, H·$[CF_2]_4$·H, b. p. 38·5°, CF_3·CH_2·CH_2·CF_3 b. p. 24°). The compound which would be expected by addition of hydrogen to the double bond, *i.e.*, 1 : 2 : 3 : 3 : 4 : 4-hexafluoro*cyclo*butane (b. p. 27°, Buxton and Tatlow, *J.*, 1954, 1177) was not produced. The structure of the hexafluorobutane was proved by its photochemical chlorination to give 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, dechlorination of which yields hexafluorobutadiene (*J.*, 1952, 4423).

Two interpretations of this rearrangement reaction are possible. The more probable is that hydrogen iodide reacts more readily with hexafluorobutadiene than with perfluoro*cyclo*butene, and thus converts the diene present in equilibrium with the *cyclo*butene into compounds such as CF_2I·CHF·CF:CF_2, CF_2I·CF:CF·CHF_2, CHF_2·CHF·CF:CF_2, or CHF_2·CF:CF·CHF_2. These compounds will be reduced further to give 1 : 1 : 2 : 3 : 4 : 4-hexafluorobutane, and in this way the continuous removal of hexafluorobutadiene from the equilibrium mixture, at a temperature where hexafluoro*cyclo*butene itself is not attacked by hydrogen iodide or by its decomposition products hydrogen and iodine, leads to almost quantitative conversion of hexafluoro*cyclo*butene into the hexafluorobutane.

A second and somewhat less probable scheme is that addition of hydrogen iodide to the double bond is followed, at the elevated reaction temperatures used, by carbon–iodine bond cleavage and rearrangement of the free radical; this is followed by reduction :





Perfluoro*cyclo*butene is readily prepared in high yield from chlorotrifluoroethylene, and its reaction with hydrogen iodide followed by chlorination and then dechlorination thus provides a convenient synthesis of perfluorobutadiene which can be applied on a larger scale than that described earlier [CF_2:$CFCl \xrightarrow{ICl} CF_2Cl$·$CFClI \xrightarrow[\text{or Hg, } h\nu]{\text{Zn, dioxan}} (CF_2Cl$·$CFCl)_2 \longrightarrow C_4F_6$; *J.*, 1952, 4423]. The rearrangement reaction is clearly capable of extension to the synthesis of other polyfluoro- and polyfluorochloro-dienes and studies in this connection will be reported later.

Scherer (U.S.P. 2,676,193; *Chem. Abs.*, 1953, **47**, 6435) has reported that 1 : 2-dichlorodifluoroethylene is dimerised by heat to give (I) or (II) or a mixture of the two. *cis-trans*-Isomerism is clearly possible in (I) and (II). The results of our own studies carried out several years ago on this reaction show that (I) is formed predominantly and probably almost exclusively; its stereochemical nature is unknown.

(I) CFCl:CF·CFCl·$CFCl_2$ CF_2Cl·CFCl·CCl:CFCl (II)

The dimerisation of 1 : 2-dichlorodifluoroethylene is readily effected in a sealed vessel or by passage of the olefin through a hot tube. Small amounts of what are probably trimers are also produced. The dimer must contain chlorine on adjacent carbon atoms, since when it is treated with zinc and dioxan, a diene $C_4Cl_2F_4$ is produced in good yield by loss of chlorine but not of fluorine; such a diene could arise from (I) or (II). The dimer contains one double bond, since it absorbs chlorine or bromine to give $C_4Cl_6F_4$ or $C_4Br_2Cl_4F_4$ respectively. Clear proof that the dimer is (I) and not (II), and hence that the diene is (III) and the chlorinated and brominated products are (IV) and (V), comes from alkaline permanganate oxidation of the dimer to give the trichlorodifluoropropionic acid (VI). This oxidation must be carried out at a pH <10 to prevent further breakdown of (VI) into dichlorofluoroacetic acid and oxalic acid; some breakdown

of (VI) occurs even with such pH control, but a 74% yield of αββ-trichlorodifluoropropionic acid was obtained under the best conditions. This shows that the double bond in the dimer is terminal and that (II), which would give the dichlorotrifluoropropionic acid (VII), is not formed. There is no reason to expect that (VII) would be less stable than (VI) and hence preferentially degraded during the oxidation; in fact, the reverse would be the

$CFCl{:}CF{\cdot}CF{:}CFCl$ (III) $\quad CFCl_2{\cdot}CFCl{\cdot}CFCl{\cdot}CFCl_2$ (IV) $\quad CFClBr{\cdot}CFBr{\cdot}CFCl{\cdot}CFCl_2$ (V)

$CFCl_2{\cdot}CFCl{\cdot}CO_2H$ (VI) $\quad CF_2Cl{\cdot}CFCl{\cdot}CO_2H$ (VII)

case, since increased fluorine content increases the stability of a polyhalogeno-acid. The presence of polyhalogenobut-2-enes formed either by the initial reaction or by allylic rearrangement [(I) $\rightleftharpoons CFCl_2{\cdot}CF{:}CF{\cdot}CFCl_2$] would explain the loss of material during the oxidation, but the ease of chlorination and bromination of the dimer shows that polyhalogenobut-2-enes are not present. Such compounds add chlorine or bromine only with difficulty and without allylic rearrangement, and preferential halogenation of the but-1-ene would thus be expected; the olefin recovered from the reaction of the dimer with less than a molar equivalent of halogen was identical with the original dimer however. All these points suggest that the dichlorodifluoroethylene dimer is very largely, and probably completely, (I).

The constitution of (VI) is proved by the formation of 1 : 2-dichlorodifluoroethylene by pyrolysis of its anhydrous sodium salt. This reaction, which has been applied to the salts of perfluoro-mono- and -di-basic acids (*J.*, 1952, 4259; 1954, 4026) and appears to be of general application with polyhalogeno-acids, is believed to proceed *via* a fluoro-carbanion :

$$CFCl_2{\cdot}CFCl{\cdot}CO_2Na \longrightarrow CFCl_2{\cdot}CFCl{\cdot}CO_2^- \longrightarrow CFCl_2{\cdot}CFCl^- + CO_2$$

$$Cl{-}CFCl{-}CFCl^- \longrightarrow Cl^- + CFCl{:}CFCl$$

The acid (VII) would have given chlorotrifluoroethylene by this procedure. Further proof of structure is given by conversion of the acid into 1 : 1 : 2 : 2-tetrachlorodifluoroethane by reaction of its silver salt with chlorine (cf. *J.*, 1951, 584; 1952, 4259) :

$$CFCl_2{\cdot}CFCl{\cdot}CO_2Ag \xrightarrow{Cl_2} CFCl_2{\cdot}CFCl_2 + CO_2 + AgCl$$

The following schemes are possible for the thermal dimerisation of 1 : 2-dichlorodifluoroethylene or 1 : 2-dichloroethylene which similarly yields $CHCl_2{\cdot}CHCl{\cdot}CH{:}CHCl$ (Bauer, U.S.P. 2,267,712/1942) :

Scheme A.

$$CFCl{:}CFCl \longrightarrow CFCl{:}CF{\cdot} + Cl{\cdot}$$

$$CFCl{:}CF{\cdot} + CFCl{:}CFCl \longrightarrow CFCl{:}CF{\cdot}CFCl{\cdot}CFCl{\cdot}$$

$$CFCl{:}CF{\cdot}CFCl{\cdot}CFCl{\cdot} + CFCl{:}CFCl \longrightarrow CFCl{:}CF{\cdot}CFCl{\cdot}CFCl_2 + CFCl{:}CF{\cdot} \longrightarrow \text{etc.}$$

This involves a chain reaction with regeneration of the $CFCl{:}CF$ radical. The compound (II) would be formed if the $CFCl{:}CCl$ radical were produced by loss of fluorine instead of chlorine.

Scheme B. A non-chain reaction would be obtained by dimerisation of the $CFCl{:}CF$ radicals :

$$CFCl{:}CF{\cdot} \longrightarrow CFCl{:}CF{\cdot}CF{:}CFCl \xrightarrow{Cl_2} CFCl_2{\cdot}CFCl{\cdot}CF{:}CFCl$$

but one would have to assume either that thermal chlorination of the diene gave only 1 : 2-addition, which is unlikely in view of experiments on the halogenation of perfluorobutadiene (*J.*, 1952, 4423), or that allylic rearrangement ($CFCl_2{\cdot}CF{:}CF{\cdot}CFCl_2 \rightleftharpoons CFCl_2{\cdot}CFCl{\cdot}CF{:}CFCl$) converted the 1 : 4-addition product into the presumedly more stable 1 : 2-addition product.

Scheme C. The radical $CFCl_2{\cdot}CFCl$ can be visualised as a chain carrier :

$$Cl{\cdot} + CFCl{:}CFCl \longrightarrow CFCl_2{\cdot}CFCl{\cdot}$$

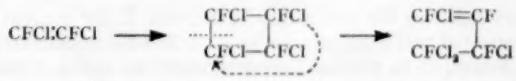
$$CFCl_2{\cdot}CFCl{\cdot} + CFCl{:}CFCl \longrightarrow CFCl_2{\cdot}CFCl{\cdot}CFCl{\cdot}CFCl{\cdot}$$

$$CFCl_2{\cdot}CFCl{\cdot}CFCl{\cdot}CFCl{\cdot} + CFCl{:}CFCl \longrightarrow CFCl_2{\cdot}CFCl{\cdot}CF{:}CFCl + CFCl_2{\cdot}CFCl{\cdot}$$

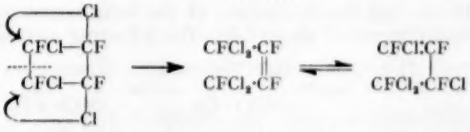
Scheme D. Combination of two radicals, each relatively stable (cf. *J.*, 1953, 1764; *J.*, 1952, 2504 *et seq.*) :

$$CFCl{:}CF\cdot + CFCl_2\cdot CFCl\cdot \longrightarrow CFCl_2\cdot CFCl\cdot CF{:}CFCl$$

Scheme E. Formation of a *cyclo*butane followed by chlorine migration and C–C cleavage :



or



The *cyclo*butane need be formed only as a transition complex in a bimolecular reaction.

Some distinction between these schemes can be made by consideration of the open-chain dimerisation of other polyhalogeno-ethylenes. Miller (*op. cit.*) has shown that pyrolysis of chlorotrifluoroethylene gives 1 : 2-dichlorohexafluoro*cyclo*butane at lower temperatures and 3 : 4-dichlorohexafluorobut-1-ene at higher temperatures. Application of Scheme A to the last reaction would give

$$CF_2{:}CFCl \longrightarrow CF_2{:}CF\cdot + Cl\cdot$$
$$CF_2{:}CF\cdot + CF_2{:}CFCl \longrightarrow CF_2{:}CF\cdot CF_2\cdot CFCl\cdot$$
$$CF_2{:}CF\cdot CF_2\cdot CFCl\cdot + CF_2{:}CFCl \longrightarrow CF_2{:}CF\cdot CF_2\cdot CFCl_2 + CF_2{:}CF\cdot$$

The direction of attack of a free radical on chlorotrifluoroethylene is well established as exclusively on the CF_2 group (*J.*, 1953, 1592). Thus Scheme A would give 4 : 4-dichlorohexafluorobut-1-ene, and Miller does not find this as a reaction product. Allylic rearrangement of the 4 : 4- into the 3 : 4-dichlorobutene is implausible, and Scheme A is thus unsatisfactory for application to chlorotrifluoroethylene and hence for 1 : 2-dichlorodifluoroethylene. Mechanisms involving homolytic fission of a C–F bond are unlikely and are not considered. Scheme B would give hexafluorobutadiene by combination of two $CF_2{:}CF$ radicals, and provided that the allylic rearrangement $CF_2Cl\cdot CF{:}CF\cdot CF_2Cl \rightleftharpoons CF_2{:}CF\cdot CFCl\cdot CF_2Cl$ gave only the 3 : 4-dichloro-compound at high temperature, would account for the dimerisation product. A chlorination reaction involving free chlorine atoms or molecules of the type postulated in Scheme B is unlikely to give only the butene and no compounds formed by addition of two molecules of chlorine to the diene, however, and is considered less likely than the other possible mechanisms.

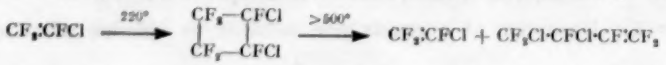
Scheme C can also be rejected, since the chlorine atom would attack the CF_2 group of chlorotrifluoroethylene to give $CF_2Cl\cdot CFCl\cdot$ and this would in turn give $CF_2Cl\cdot CFCl\cdot CF_2\cdot CFCl\cdot$. The conversion of this radical into $CF_2Cl\cdot CFCl\cdot CF{:}CF_2$ by reaction with chlorotrifluoroethylene is highly improbable.

Complete distinction between Schemes D and E cannot be made on the evidence available. Scheme D applied to chlorotrifluoroethylene would be

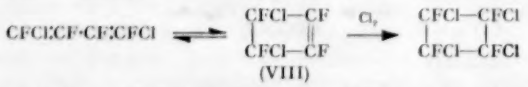
$$CF_2{:}CFCl \longrightarrow CF_2{:}CF\cdot + Cl\cdot$$
$$Cl\cdot + CF_2{:}CFCl \longrightarrow CF_2Cl\cdot CFCl\cdot$$
$$CF_2{:}CF\cdot + CF_2Cl\cdot CFCl\cdot \longrightarrow CF_2{:}CF\cdot CFCl\cdot CF_2Cl$$

and this would be in accord with the direction of radical addition to chlorotrifluoroethylene and with the stabilities of the combining radicals. Although Scheme D explains the facts, it is not considered highly probable, since other products such as those formed by self-combination of $CF_2{:}CF$ or $CF_2Cl\cdot CFCl$ radicals would be expected. It is thus concluded that the open-chain dimerisation of chlorotrifluoroethylene is not a free-radical process but a bimolecular reaction possibly involving a *cyclo*butane intermediate as in Scheme E. It seems probable that 1 : 2-dichlorodifluoroethylene dimerisation occurs by a similar

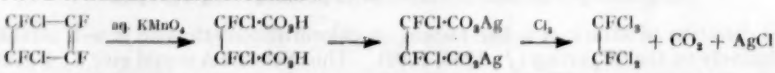
process. Some support for the application of Scheme E to chlorotrifluoroethylene dimerisation is given by the pyrolysis of 1 : 2-dichlorohexafluoro*cyclo*butane, which yields both chlorotrifluoroethylene and 3 : 4-dichlorohexafluorobut-1-ene (Miller, *op. cit.*) :



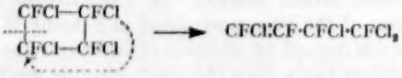
To throw further light on the possibility of Scheme E for general application to the open-chain dimerisation of polyhalogeno-olefins, 1 : 2 : 3 : 4-tetrachlorotetrafluoro*cyclo*butane was synthesised. Attempts to prepare this compound by cyclic dimerisation of 1 : 2-dichlorodifluoroethylene failed, but the realisation of the hexafluorobutadiene ⇌ hexafluoro*cyclo*butene equilibrium reported above led to the following successful synthesis :



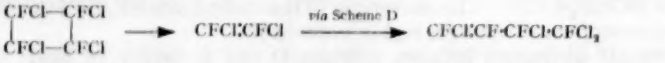
The interconversion diene ⇌ *cyclo*butene is probably a general reaction for polyhalogeno-compounds. The equilibrium lies in favour of the *cyclo*butene, and can be approached from either compound with the formation of only relatively small amounts of products with a higher b. p. The conversion of the *cyclo*butene into the diene shows that halogen migration has not occurred during rearrangement of the diene into the *cyclo*butene; compounds such as 1 : 4-, 1 : 3-, or 1 : 2-dichlorotetrafluoro*cyclo*butene are not produced. Further proof is given by the aqueous permanganate oxidation of (VIII) to give αβ-dichloro-αβ-difluorosuccinic acid, isolated as its silver salt and thence converted into 1 : 1 : 2 : 2-tetrachlorodifluoroethane :



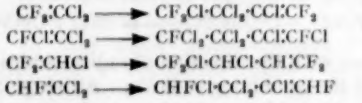
Chlorine adds smoothly to 2 : 3-dichlorotetrafluoro*cyclo*butene to give 1 : 2 : 3 : 4-tetrachlorotetrafluoro*cyclo*butane. Reaction of the last compound with zinc and dioxan gives the *cyclo*butene again, but attempts to remove a second molecule of chlorine to give perfluoro*cyclo*buta-1 : 3-diene failed. Pyrolysis of the tetrachlorotetrafluoro*cyclo*butane gives moderate yields of 1 : 3 : 4 : 4-tetrachlorotetrafluorobut-1-ene (I), and this supports Scheme E as the method of open-chain dimerisation of polyhalogeno-ethylenes by a non-radical mechanism :



although it should be noted that free-radical Scheme D proceeding with initial formation of 1 : 2-dichlorodifluoroethylene would give the same product :



The open-chain dimerisation of other polyhalogeno-ethylenes by a non-radical mechanism can now be predicted with reasonable certainty according to Scheme E provided that (*a*) the olefin contains fluorine and (*b*) peroxides are absent, *e.g.*,



It cannot be emphasised too strongly that a free-radical dimerisation of polyhalogeno-ethylenes can very probably be achieved also, *e.g.*, by use of a peroxide initiator with olefins which do not give long-chain polymers readily under free-radical conditions. The direction of addition of a free radical to $\dot{C}FCl{:}CCl_2$, $\dot{C}F_2{:}CHCl$, and $\dot{C}HF{:}CCl_2$, which

falls into this category, is known to be at the carbon atom indicated by an asterisk (unpublished results), and a free radical R produced from a peroxide would abstract chlorine and so enable Scheme A to operate :

$$CFCl{:}CCl_2 \xrightarrow{R\cdot} CFCl{:}CCl\cdot \xrightarrow{CFCl{:}CCl_2} CFCl{:}CCl{\cdot}CFCl{\cdot}CCl_2\cdot \xrightarrow{CFCl{:}CCl_2} CFCl{:}CCl{\cdot}CFCl{\cdot}CCl_3 + CFCl{:}CCl\cdot$$

$$CF_2{:}CHCl \xrightarrow{R\cdot} CF_2{:}\dot{C}H \xrightarrow{CF_2{:}CHCl} CF_2{:}CH{\cdot}CF_2{\cdot}CHCl\cdot \xrightarrow{CF_2{:}CHCl} CF_2{:}CH{\cdot}CF_2{\cdot}CHCl_2 + CF_2{:}CH\cdot$$

or

$$CF_2{:}CHCl \xrightarrow{R\cdot} CF_2{:}CCl\cdot \xrightarrow{CF_2{:}CHCl} CF_2{:}CCl{\cdot}CF_2{\cdot}CHCl\cdot \xrightarrow{CF_2{:}CHCl} CF_2{:}CCl{\cdot}CF_2{\cdot}CH_2Cl + CF_2{:}CCl\cdot$$

$$CHF{:}CCl_2 \xrightarrow{R\cdot} CHF{:}CCl\cdot \xrightarrow{CHF{:}CCl_2} CHF{:}CCl{\cdot}CHF{\cdot}CCl_2\cdot \xrightarrow{CHF{:}CCl_2} CHF{:}CCl{\cdot}CHF{\cdot}CCl_3 + CHF{:}CCl\cdot$$

Open-chain dimers different from those obtainable by purely thermal non-radical dimerisation are thus possible.

This possibility is being investigated, but there is some indication in the literature that trichloroethylene can give two dimers. When it is heated at 210° under 40 atm. pressure in presence of antioxidants the dimer obtained is believed to be $CCl_2{\cdot}CHCl{\cdot}CH{:}CCl_2$ (Rodd, "Chemistry of Carbon Compounds," Elsevier, 1951, Vol. IA, p. 283; French P. 814,423/1937, 51,288/1942; G.P. 721,380/1942; Mugden and Wimmer, G.P. 736,232/1943; U.S.P. 2,338,297/1944), although no precise proof of structure is available. This could be obtained by Scheme E :

$$CHCl{:}CCl_2 \longrightarrow \begin{matrix} CCl_2{-}CHCl \\ | \quad\quad | \\ CCl_2{-}CHCl \end{matrix} \longrightarrow CCl_2{:}CH{\cdot}CHCl{\cdot}CCl_3$$

The dimer obtained when trichloroethylene is heated in presence of peroxides such as benzoyl peroxide is probably $CHCl_2{\cdot}CCl_2{\cdot}CH{:}CCl_2$ or its allylic rearrangement product ($CHCl_2{\cdot}CCl_2{\cdot}CH{:}CCl_2 \rightleftharpoons CHCl_2{\cdot}CCl{:}CH{\cdot}CCl_3 \rightleftharpoons CHCl{:}CCl{\cdot}CHCl{\cdot}CCl_3$) (G.P. 718,057/1942; French P. 841,728/1939; B.P. 517,213/1940). Henne and Ruh (*J. Amer. Chem. Soc.*, 1947, **69**, 279) have produced evidence in support of this constitution, but it should be noted that their evidence rests upon the formation of $CF_2Cl{\cdot}CCl_2{\cdot}CCl_2{\cdot}CCl_3$ by the sequence

$$CHCl_2{\cdot}CCl_2{\cdot}CH{:}CCl_2 \xrightarrow{Cl_2} CHCl_2{\cdot}CCl_2{\cdot}CHCl{\cdot}CCl_3 \xrightarrow{HF} CHCl_2{\cdot}CCl_2{\cdot}CHCl{\cdot}CF_2Cl$$

$$CHCl_2{\cdot}CCl_2{\cdot}CHCl{\cdot}CF_2Cl \xrightarrow{KOH} CHCl_2{\cdot}CCl{:}CCl{\cdot}CF_2Cl \xrightarrow{Cl_2} CHCl_2{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_2Cl$$

$$CHCl_2{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_2Cl \xrightarrow{NaOH} CCl_2{:}CCl{\cdot}CCl_2{\cdot}CF_2Cl \xrightarrow{Cl_2} CCl_2{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_2Cl$$

but none of the constitutions of the intermediates was proved, and neither yields nor analyses was given. The formation of $CF_2Cl{\cdot}CCl_2{\cdot}CCl_2{\cdot}CCl_3$ could equally well be used as evidence for $CCl_3{\cdot}CHCl{\cdot}CH{:}CCl_2$ if the not-impossible replacement of two chlorine atoms on one carbon atom by fluorine occurred :

$$CCl_2{\cdot}CHCl{\cdot}CH{:}CCl_2 \xrightarrow{Cl_2} CCl_3{\cdot}CHCl{\cdot}CHCl{\cdot}CCl_3 \xrightarrow{HF} CCl_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_2Cl$$

$$CCl_3{\cdot}CHCl{\cdot}CHCl{\cdot}CF_2Cl \xrightarrow{KOH} CCl_2{:}CCl{\cdot}CHCl{\cdot}CF_2Cl \xrightarrow{Cl_2} CCl_3{\cdot}CCl_2{\cdot}CHCl{\cdot}CF_2Cl$$

$$CCl_3{\cdot}CCl_2{\cdot}CHCl{\cdot}CF_2Cl \xrightarrow{NaOH} CCl_2{\cdot}CCl{:}CCl{\cdot}CF_2Cl \xrightarrow{Cl_2} CCl_3{\cdot}CCl_2{\cdot}CCl_2{\cdot}CF_2Cl$$

If Henne and Ruh's conclusions about the constitution of peroxide-produced trichloroethylene dimer are accepted, however, the most probable method of formation is by Scheme A :

$$CHCl{:}CCl_2 \xrightarrow{R\cdot} CHCl{:}CCl\cdot \xrightarrow{CHCl{:}CCl_2} CHCl{:}CCl{\cdot}CHCl{\cdot}CCl_2\cdot$$

$$CHCl{:}CCl{\cdot}CHCl{\cdot}CCl_2\cdot \xrightarrow{CHCl{:}CCl_2} CHCl{:}CCl{\cdot}CHCl{\cdot}CCl_3 + CHCl{:}CCl\cdot \longrightarrow \text{etc.}$$

$$CHCl{:}CCl{\cdot}CHCl{\cdot}CCl_3 \rightleftharpoons CHCl_2{\cdot}CCl{:}CH{\cdot}CCl_3 \rightleftharpoons CHCl_2{\cdot}CCl_2{\cdot}CH{:}CCl_2$$

The direction of addition of a free radical to trichloroethylene is known to be to the CHCl group (G. F. Liptrot and B. R. Steele, unpublished results), and the formation of

$CHCl{:}\dot{C}Cl$ by attack of R on trichloroethylene rather than the less stable $\dot{C}Cl_2{:}CH$ is plausible.

The concept of two reaction schemes, the first non-radical and possibly with a *cyclo*butane as intermediate, the second free radical, for dimerisation of polyhalogeno-ethylenes must be adopted, since no single mechanism can be put forward to explain all the known dimerisations without unreasonable assumptions. It will clearly not be possible to make any one of the reaction schemes operate at will with every olefin, but it should be possible to demonstrate both mechanisms by careful choice of olefin; experiments along these lines will be reported later.

Experimental

Reactions were carried out in sealed Pyrex or silica tubes unless otherwise stated, with precautions to exclude moisture, air, or materials which might catalyse ionic or free-radical reactions.

*Reaction of Hydrogen Iodide with Perfluoro*cyclo*butene.*—Perfluoro*cyclo*butene and hydrogen iodide failed to react when heated in a sealed tube at 210° (65 hr.). Perfluoro*cyclo*butene (1·14 g.) and hydrogen iodide (4·99 g.), heated at 275° (24 hr.) in a sealed tube, gave unchanged olefin (0·41 g.) and 1 : 1 : 2 : 3 : 4 : 4-*hexafluorobutane* (90%), b. p. 63—65°, n_D^{20} 1·300 (Found: C, 28·6; H, 2·4%; *M*, 166. $C_4H_4F_6$ requires C, 28·8; H, 2·4%; *M*, 166).

In a second experiment, perfluoro*cyclo*butene (2·0 g.) and a 20% excess of hydrogen iodide, heated at 300° (24 hr.), gave 1 : 1 : 2 : 3 : 4 : 4-hexafluorobutane (98%) and unchanged olefin (<2%). Iodine was liberated during the reaction, but no polymerisation or etching of the glass tube was apparent.

The reaction was also carried out successfully in an autoclave. Perfluoro*cyclo*butene (15·0 g.) and hydrogen iodide (100% excess) in a stainless-steel autoclave were heated in an oil-bath at 290—300° (32 hr.) to give 1 : 1 : 2 : 3 : 4 : 4-hexafluorobutane (92%) and perfluoro*cyclo*butene (4%). There was no liberation of hydrogen fluoride or carbon.

Further experiments gave yields of 88—93% of the hexafluorobutane from 15—20 g. of perfluoro*cyclo*butene. Careful control of reaction temperature is necessary to prevent formation of hydrogen fluoride.

Conversion of 1 : 1 : 2 : 3 : 4 : 4-*Hexafluorobutane into Hexafluorobutadiene.*—The hexafluorobutane (5·3 g.), chlorine (100% excess), and water (4 ml.) in a silica tube were exposed to ultraviolet light (24 hr.) to give 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (93%), b. p. 134°, n_D^{22} 1·382 (Found: C, 15·8. Calc. for $C_4Cl_4F_6$: C, 15·8%). The infrared spectrum of the chloro-compound was identical with that of a known sample (*J.*, 1952, 4423). Final proof of structure was given by reaction of the tetrachlorohexafluorobutane (6·5 g.) with zinc (30 g.) and refluxing ethanol (80 ml.) (6 hr.) to give perfluorobutadiene (87%), b. p. 5·8° (Found: *M*, 162. Calc. for C_4F_6: *M*, 162). The infrared spectrum of the perfluorobutadiene was identical with that of a known sample (*J.*, 1952, 4423).

*Isomerisation of Perfluoro*cyclo*butene and Perfluorobutadiene.*—When perfluoro*cyclo*butene (5·6 g.) was passed through a silica tube packed with active carbon flakes, heated to 580° over a 12″ length, examination of the reaction products by infrared spectroscopy revealed the presence of perfluoro*cyclo*butene (89%), perfluorobutadiene (8%), and unidentified material of higher b. p., probably dimers and trimers. Experiments at 550°, 600°, 650°, and 700° gave 3, 10, 12, and 6% yields of perfluorobutadiene, respectively. Final identification of the diene was made by treatment of the combined reaction products with an excess of chlorine with exposure to ultraviolet light (12 hr.) to give 1 : 2-dichlorohexafluoro*cyclo*butane, b. p. 60°, and 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, b. p. 133—134°. The infrared spectrum of the last compound was identical with that of a known specimen; furthermore, the tetrachloro-compound gave perfluorobutadiene (85%) (identified spectroscopically) when treated with zinc and refluxing ethanol.

Hexafluorobutadiene (3·9 g.), passed through the tube used above at 580°, gave perfluoro*cyclo*butene (80%) and perfluorobutadiene (10%). Experiments at 600°, 640°, and 690° gave 82, 78, and 84% yields of perfluoro*cyclo*butene, respectively, with perfluorobutadiene as the other major product, though small amounts of dimers and trimers were also detected. The reaction product from the experiment at 580° was photochemically chlorinated (12 hr.) to give 1 : 2-dichlorohexafluoro*cyclo*butane, b. p. 59°, and 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, b. p. 132—134°. The identity of the dichlorohexafluoro*cyclo*butane was confirmed by means of its infrared spectrum.

Dimerisation of 1 : 2-*Dichlorodifluoroethylene.*—(a) *In silica tubes.* The olefin (6·7 g.), heated in a silica tube at 230° (24 hr.), gave unchanged olefin (31%) and its dimer $C_4Cl_4F_6$ (69% based on olefin used), b. p. 140—142°. Similar experiments at 250°, 280°, and 300° gave 73, 66, and 61% yields of dimer, respectively. At the higher temperatures very little original olefin was recovered unchanged but there was an increase in the amount of breakdown products.

(b) *In an autoclave.* Dichlorodifluoroethylene (10·7 g.) was heated at 260° in a 20 ml. autoclave (15 hr.) to give the dimer (71% based on olefin used), unchanged olefin (12%), and intermediate fractions. The combined still residues were distilled to give material believed to contain trimers, but these were not investigated further.

(c) *Properties and reactions of the dimer.* The combined dimer fraction from the above experiments was redistilled to give 1 : 3 : 4 : 4-*tetrachlorotetrafluorobut*-1-*ene*, b. p. 140·5—141°, n_D^{20} 1·429 (Found : C, 18·0; Cl, 52·9. $C_4Cl_4F_6$ requires C, 18·0; Cl, 53·4%). A sample of the dimer (1·3 g.), treated with an excess of chlorine in a silica tube exposed to ultraviolet light, gave 1 : 1 : 2 : 3 : 4 : 4-hexachlorotetrafluorobutane (97%) (Found : C, 14·2. Calc. for $C_4Cl_6F_4$: C, 14·2%), b. p. 207—208°, n_D^{20} 1·457. Miller (*loc. cit.*) prepared this compound in 32% yield by reaction of hexachlorobutadiene and fluorine, and reports b. p. 133—134°/100 mm., n_D^{20} 1·4568.

A sample of the dimer $C_4Cl_4F_6$ (3·3 g.), mixed with bromine (20% excess), heated to 50°, and exposed to ultraviolet light (8 hr.), gave 1 : 2-dibromo-1 : 3 : 4 : 4-tetrachlorotetrafluorobutane (83%), b. p. 138—140°/35 mm., n_D^{20} 1·493.

1 : 3 : 4 : 4-Tetrachlorotetrafluorobut-1-ene (6·8 g.), dissolved in dioxan (10 ml.), was added dropwise to zinc (20 g.) and refluxing dioxan (50 ml.) in an apparatus fitted with reflux condenser and take-off so that the reflux liquid could be steadily removed (5 hr.) and dropped into an excess of water. The diene produced by the dehalogenation was thus removed, with dioxan, from the reaction vessel and prevented from being reduced by prolonged contact with the zinc. The lower layer obtained in this way was shaken with water to remove last traces of dioxan and distilled from phosphoric anhydride to give 1 : 4-dichlorotetrafluorobutadiene (78%), b. p. 79°, n_D^{20} 1·403 (Found : C, 20·6; Cl, 30·7%; *M*, 233. Calc. for $C_4Cl_2F_6$: C, 20·6; Cl, 30·5%; *M*, 233). Miller (*loc. cit.*) gives b. p. 78° for this diene.

The same diene was produced in 81% yield when 1 : 1 : 2 : 3 : 4 : 4-hexachlorotetrafluorobutane (4·7 g.) was treated with zinc and dioxan under the same conditions as used above. The dibromo-compound described above (3·9 g.) similarly gave a 75% yield of 1 : 4-dichlorotetrafluorobutadiene.

αββ-*Trichlorodifluoropropionic Acid.*—1 : 3 : 4 : 4-Tetrachlorotetrafluorobut-1-ene (5·9 g.), potassium permanganate (6·0 g.), and water (50 ml.) were heated at 80° under a reflux condenser (8 hr.). The pH of the solution was kept at 7—8·5 by periodic addition of 5% aqueous sodium hydroxide; this was found necessary to prevent extensive breakdown of the chain when more alkaline solutions were used. The excess of permanganate was destroyed by treatment with sulphur dioxide, and the solution was extracted by ether in the usual way (cf. *J.*, 1950, 3037, 2789; 1952, 4259; 1953, 1548). Distillation of the dried ethereal extracts gave a small amount (0·4 g.) of an acid containing fluorine and chlorine which was possibly dichlorofluoroacetic acid, but was not definitely identified, b. p. 90—95°/25 mm., and αββ-*trichlorodifluoropropionic acid* (74%), b. p. 115—118°/25 mm., 95—96°/5 mm. (Found : C, 16·9; H, 0·6; Cl, 49·5%; equiv., 215. $C_3HO_2Cl_3F_2$ requires C, 16·9; H, 0·5; Cl, 49·9%; equiv., 213·5). The acid is a solid at room temperature.

Sodium αββ-trichlorodifluoropropionate (3·2 g.), prepared by exact neutralisation of the acid followed by freeze-drying, was thoroughly dried *in vacuo* over phosphoric anhydride (7 days), then spread in a thin layer on a platinum sheet which was placed inside a steel tube. The tube was closed at one end, and the other end led to an oil pump *via* a trap cooled in liquid oxygen. The apparatus was evacuated to 10^{-2} mm. and the closed end of the tube was slowly pushed (1 hr.) into a furnace at 300°. In this way pyrolysis of the sodium salt was effected at the lowest possible temperature and the products were immediately removed from the reaction zone. Distillation gave carbon dioxide and 1 : 2-dichlorodifluoroethylene (84%), b. p. 21—22°, identified spectroscopically. The residue on the platinum sheet was sodium chloride containing only a trace of sodium fluoride.

Silver αββ-trichlorodifluoropropionate (2·1 g.), prepared by neutralisation of the acid with silver carbonate followed by filtration and freeze-drying, was dried *in vacuo* then sealed with an excess of chlorine in a Pyrex tube. Reaction occurred at 20°, and was completed at 40°. Distillation of the volatile products gave 1 : 1 : 2 : 2-tetrachlorodifluoroethane (79%), b. p. 92—93°, n_D^{20} 1·413 (Found : *M*, 205. Calc. for $C_2Cl_4F_2$: *M*, 204), identified spectroscopically.

Rearrangement of 1 : 4-*Dichlorotetrafluorobutadiene.*—The diene (3·9 g.), heated at 250° in

a sealed tube (12 hr.), gave unchanged diene (12%), 2 : 3-*dichlorotetrafluoro*cyclo*butene* (56%), b. p. 65·5°, n_D^{20} 1·375 (Found : C, 20·4; Cl, 30·0%; *M*, 233. $C_4Cl_2F_4$ requires C, 20·6; Cl, 30·5%; *M*, 233), and products of higher b. p. believed to be dimers. The presence of a double bond in the *cyclo*butene was shown by its reaction with chlorine (10% excess) on exposure to ultraviolet light to give 1 : 2 : 3 : 4-tetrachlorotetrafluoro*cyclo*butane (95%), b. p. 129°, m. p. 45—46°. The tetrachloro-compound was reconverted into 2 : 3-dichlorotetrafluoro-*cyclo*butene in 83% yield by reaction with zinc and refluxing ethanol with continuous removal of the olefin; this shows that no rearrangement occurred during the photochemical chlorination.

Attempts were made to dechlorinate 2 : 3-dichlorotetrafluoro*cyclo*butene by reaction with zinc and dioxan in a sealed tube at 120°, 150°, and 180°. There was only slight reaction at 120°, and the products from the reactions at the higher temperatures contained hydrogen; none of the products corresponded to a tetrafluoro*cyclo*butadiene.

1 : 4-Dichlorotetrafluorobutadiene was also converted into the dichlorotetrafluoro*cyclo*-butene by passage through a hot tube. The diene (4·7 g.), passed through a platinum tube packed with active carbon at 320° (2 hr.), gave a 74% yield of the *cyclo*butene; unchanged diene and products of higher b. p. were also detected.

2 : 3-Dichlorotetrafluoro*cyclo*butene (3·4 g.), passed through a platinum tube packed with active carbon at 380°, gave unchanged dichlorotetrafluoro*cyclo*butene (70%), 1 : 4-dichlorotetra-fluorobutadiene (14%), and unidentified products of higher b. p. After initial separation by distillation, the *cyclo*butene and the diene were chlorinated to show the presence of one and two double bonds respectively, and to confirm their identity with the compounds previously described.

αβ-*Dichloro*-αβ-*difluorosuccinic Acid.*—2 : 3-Dichlorotetrafluoro*cyclo*butene (3·8 g.), water (15 ml.), and potassium permanganate (4 g.) were heated at 70° in a stainless-steel autoclave (10 hr.). There was no unchanged *cyclo*butene. The aqueous solution was treated with sulphur dioxide and extracted with ether in the usual way. Distillation of the material remaining after removal of the ether gave αβ-*dichloro*-αβ-*difluorosuccinic acid* (62%), b. p. 100—105°/0·1 mm. (Found : equiv., 112·5. $C_4H_2O_4Cl_2F_2$ requires equiv., 111·5). This was neutralised with a slight excess of silver carbonate, and filtration and freeze-drying of the aqueous solution gave *silver* αβ-*dichloro*-αβ-*difluorosuccinate* (Found : Ag, 49·0. $C_4O_4Cl_2F_2Ag_2$ requires Ag, 49·4%).

Reaction of the silver salt (0·8 g.) with a 10% excess of chlorine in a sealed tube at 30° gave 1 : 1 : 2 : 2-tetrachlorodifluoroethane (71%), b. p. 92° (isoteniscope) (Found : *M*, 203. Calc. for $C_2Cl_4F_2$: *M*, 204), identified spectroscopically.

Pyrolysis of 1 : 2 : 3 : 4-*Tetrachlorotetrafluoro*cyclo*butane.*—The *cyclo*butane (5·3 g.), passed through a platinum tube packed with active charcoal and heated to 350°, gave 1 : 3 : 4 : 4-tetra-chlorotetrafluorobut-1-ene (57%), 1 : 2-dichlorodifluoroethylene (11%), and unidentified products, b. p. 50—100°.

The *cyclo*butane (3·1 g.), heated in a silica tube at 290°, gave 1 : 3 : 4 : 4-tetrachlorotetra-fluorobut-1-ene (51%), unchanged 1 : 2 : 3 : 4-tetrachlorotetrafluoro*cyclo*butane (22%), a small amount of 1 : 2-dichlorodifluoroethylene (9%), and unidentified products.

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An Investigation of Complex Formation by Partition of a Reactant between the Vapour Phase and Solution: The Determination of Association Constants and the Heats of Formation of Some Hydrogen Bonds.

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A method of investigating complex formation between a volatile reactant and an involatile one in a volatile solvent, which involves partitioning between the liquid and the vapour phase, is described. It has been used to investigate hydrogen bonding between trimethylamine and some hydroxy-compounds, amines, and thiophenol. A regular variation in the association constant of the interaction is observed and cannot be explained satisfactorily. The results appear, however, to be suitable for internal comparison.

It is found that the strength of the O–H–N bond varies according to the acid strength of the OH group, and that a weak N–H–N bond is formed in some cases; no evidence for the formation of the S–H–N bond was obtained.

From measurements at different temperatures, values for ΔH can be derived; these agree quite well with values obtained calorimetrically.

Electric dipole moment measurements can, in principle, be applied to study chemical interactions between molecules. From the change in moment when a multimolecular complex is formed, information about the nature and the extent of the perturbation can be derived. Save for the stable co-ordination complexes, however, this application has not been made extensively, largely because, for the less stable ones, it is necessary to know the association constant before the electrical polarisation measurements can be fully used.

It is not generally practicable to derive both the association constant and the dipole moment of the complex from polarisation data alone (Earp and Glasstone, *J.*, 1935, 1709; Glasstone, *Trans. Faraday Soc.*, 1937, **33**, 200; Hammick, Norris, and Sutton, *J.*, 1938, 1755) though this may be done in special cases (Few and Smith, *J.*, 1949, 2781). Of the independent methods so far developed for determining the former, the most generally useful is the spectroscopic one, but this has some limitations.

The present communication describes a variant of another method of wide scope. Partitioning of a reactant between two liquids suffers from complications, particularly if one phase is aqueous (see *e.g.*, Anderson and Hammick, *J.*, 1950, 1089; Szyszkowski, *Z. phys. Chem.*, 1928, **131**, 175). If, however, one reactant (A) is volatile, the other (B) is involatile, and the solvent (S) also volatile, it is possible to partition between the liquid and the vapour phase. From a calibration it should be possible to obtain a relation between the A : S ratios in the two phases. If this were not generally affected by the presence of a third substance, then from the A : S ratio in the vapour over a solution of both A and B in S, it should be possible to obtain the ratio of free A to S in the liquid phase. If there is a specific reaction between A and B, and if the ratio of total A to S is known, the proportion of bound A can thus be derived. If then the reaction is simply: $A + B \rightleftharpoons C$ and the law of mass action is applicable, if c_A and c_B are the initial concentrations of A and of B, and c_C the concentration of the complex C, then:

$$K_{\text{assoc.}} = \frac{c_C}{(c_A - c_C)(c_B - c_C)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

From the measurements indicated, it is clearly possible to obtain K.

The fundamental assumptions are (i) that the A : S ratio in the vapour depends only on the free A : S ratio in the liquid, (ii) that the activity coefficients of the molecular species taking part in the reaction are unity, and (iii) that the complex is of the simple 1 : 1 type. Assumptions (i) and (ii) imply *inter alia* that the forces between A and B leading to complex formation are of very short range; and assumption (iii) implies that these are specific and

saturable. A further, practical requirement is that the ratio of the saturated vapour pressures, of A to B, shall be large, *i.e.*, 10 : 1 or more if possible.

A type of system which conforms to most of these requirements is that in which A is a volatile amine such as trimethylamine, B is a relatively involatile substance with a moderately acidic hydrogen atom, *e.g.*, a phenol, and S is a non-polar saturated hydrocarbon, *e.g.*, *cyclo*hexane. Moreover, the investigation of hydrogen bonding in such systems is interesting for its own sake. Accordingly, a series of them has been examined, with B = phenol, *o*-, *m*-, and *p*-cresol, *p*-chlorophenol, α- and β-naphthol, triphenylmethanol, *n*-heptyl alcohol, 2 : 5-dimethylpyrrole, indole, and benzenethiol. The results of attempts to determine association constants are described; the application of these to electrical polarisation values is dealt with in the following paper.

Experimental

Theory of the Method.—The relative amounts of the two volatile components in the vapour phase over a ternary mixture are used to deduce the term $(c_A - c_C)$ in equation (1). To do this the ratio of the two components over the ternary mixture is compared with that over their binary mixture.

Consider the case of a binary mixture containing a moles of A and s moles of S, both A and S being volatile. The respective mole fractions are:

$$f_A = a/(a + s) \qquad f_S = s/(a + s)$$

If Raoult's law is obeyed, the partial vapour pressures above the solution are: $f_A p_A^\circ$ and $f_S p_S^\circ$, where p_A° and p_S° are the saturated vapour pressures of the pure components.

The amounts of vapour carried over when a stream of gas is swept over the surface of the mixture depends upon the flow rate of the carrier gas and the degree of saturation of the gas stream with respect to each vapour; but, if the degree of saturation is independent of the flow rate, the composition of a condensate from the gas stream will also be independent of it. The amounts of A and S carried over will then be proportional to $\alpha f_A p_A^\circ$ and $\beta f_S p_S^\circ$ moles, α and β being the factors indicating departures from Raoult's law and the degree of saturation of the gas stream, assuming that they can be so expressed. The proportionality factor will be the same in each case and will depend upon the volume of carrier gas passed.

The mole fraction of A in the condensate will therefore be:

$$N_A = \frac{\alpha f_A p_A^\circ}{\alpha f_A p_A^\circ + \beta f_S p_S^\circ} = \frac{\alpha f_A p_A^\circ}{\alpha f_A p_A^\circ + \beta p_S^\circ (1 - f_A)} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This equation relates the mole fraction of A in the condensate to the mole fraction of A in the corresponding binary mixture and is the ideal equation of the calibration curve.

Consider the case of a ternary mixture, the third component, B, being involatile. Let a' moles of A, s' moles of S and b' moles of B be present, then the respective mole fractions are:

$$f_A' = a'/(a' + s' + b') \qquad f_S' = s'/(a' + s' + b')$$

Now, if the presence of B does not alter the values of α and β, the mole fraction of A in the condensate may be expressed as:

$$N_A' = \frac{\alpha f_A' p_A^\circ}{\alpha f_A' p_A^\circ + \beta f_S' p_S^\circ} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Furthermore, equation (2) holds for all values of a and s and in particular for the case where $a = a'$, $s = s'$, when

$$f_A = a'/(a' + s'),\ f_S = s'/(a' + s'),\ \textit{i.e.},\ f_A/f_S = a'/s'$$

but, also,

$$f_A'/f_S' = a'/s' \quad \therefore f_A/f_S = f_A'/f_S' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

From equations (2), (3), and (4) we have

$$N_A' = \frac{\alpha(f_A/f_S) \cdot p_A^\circ}{\alpha(f_A/f_S) \cdot p_A^\circ + \beta p_S^\circ} = N_A$$

N_A', the mole fraction of A in the condensate, may therefore be expressed in terms of $f_A = a'/(a' + s')$, *i.e.*, the mole fraction of A in the liquid mixture with respect to A and S only. If therefore the addition of B does not affect the relative activities of A and S in the ternary

mixture, the same relation between the mole fractions of A in the condensate and solution will apply as in the case of the binary mixture of A and S, providing that in the case of the ternary solution the mole fraction of A is expressed in terms of A and S only. If the addition of B affects the activity of A this will no longer be true and the deviation may be used to determine an equilibrium constant for the interaction between A and B, on the assumption that this is of a certain type and that the activity of S remains unchanged. In the theory of this determination (below) weight fractions are used instead of mole fractions, but the above treatment still applies since corresponding weight and mole fractions may be related by a factor depending only on the values of a and s and the respective molecular weights.

The algebra used in the determination of the association constant K in a particular case is straightforward but somewhat involved; so it is convenient to give it in outline as follows:

Consider a ternary solution. Let W be its total weight, W_A the total weight of A, W_A' the weight of free A, W_A'' the weight of bound A, M_A the molecular weight of A, W_S the weight of solvent, M_S the molecular weight of S, W_B the total weight of B, and M_B the molecular weight of B.

The quantities known experimentally are:

$$x_a = W_A'/(W_A' + W_S),\ y_a = W_A/W,\ y_b = W_B/W$$

Now
$$W = W_A' + W_A'' + W_S + W_B \quad \therefore x_a = \frac{W_A'}{W - (W_B + W_A'')}$$

$$\therefore \frac{W_A'}{W} = x_a\left[1 - \frac{W_B + W_A''}{W}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

But
$$\frac{W_A'}{W} = \frac{W_A - W_A''}{W} = y_a - \frac{W_A''}{W}$$

$$\therefore \frac{W_A''}{W} = \frac{y_a - x_a + (W_B/W)\,.\,x_a}{1 - x_a} = \frac{y_a - (1 - y_b)\,.\,x_a}{1 - x_a} = \gamma$$

But the molar amount of a 1 : 1 complex $= m_c = W_A''/M_A$

I.e.,
$$m_c = W\gamma/M_A \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Now the weight of free B $= Wy_b - m_cM_B$

$$\therefore \text{Molar amount of free B} = m_B = \frac{W}{M_B}\left[y_b - \frac{M_B\gamma}{M_A}\right] \quad . \quad . \quad . \quad . \quad (7)$$

Also the weight of free A $= W_A - W_A''$

$$\therefore \text{Molar amount of free A} = m_A = \frac{W}{M_A}[y_a - \gamma] \quad . \quad . \quad . \quad . \quad . \quad (8)$$

If m is the total number of moles present, by using molar fractions

$$K = \frac{(m_c/m)}{(m_A/m)\,.\,(m_B/m)} = \frac{m\,.\,m_c}{m_A\,.\,m_B}$$

Now, approximately, $m = W/M_S$

$$\therefore K = \frac{W\,.\,m_c}{M_S\,.\,m_A\,.\,m_B}$$

Whence, from equations (6), (7), and (8)

$$K = \frac{M_B}{M_S}\left\{\frac{\gamma}{(y_a - \gamma)(y_b - [M_A/M_B]\gamma)}\right\}$$

Although it is simpler for use in certain calculations, the association constant as defined above is not strictly a mass-action equilibrium constant because it involves molar fractions instead of molar concentrations. For the dilute solutions such as are used in this work, however, the following simple relation holds:

$$K_{\text{molar concn.}} = K_{\text{mol. fractn.}} \times V_s$$

where V_s is the molar volume of the solvent, which we took to be 0·1075 l. at 25°.

Apparatus and Technique.—(a) *Association constants.* In the notation of the previous section, the data required are x_a, y_a, and y_b. In our work A was in all cases trimethylamine and S *cyclo*hexane. y_a may be determined by acidimetric analysis of the reaction mixture. y_b is determined initially by weight when the reaction mixture is made up. Its value changes during an investigation, for distillation is involved and B is involatile; but, the initial weight of the solution and the amounts of A and of S removed on distillation and sampling being known, the successive values may be calculated. x_a is determined by the vapour partition method.

About 100 c.c. of the mixture were taken at the beginning of the investigation, during the course of which the volume decreased to about 50 c.c. The initial mixture was prepared by diluting approximately 10 times with dry *cyclo*hexane a stock solution of trimethylamine in *cyclo*hexane containing about 8% of trimethylamine by weight. In the investigation of a ternary mixture the involatile component B was weighed into the diluted solution and dissolved, the mixture was transferred to the saturator, and the weight so transferred determined by difference.

The mixture was shaken in a horizontal tubular glass vessel, having indentations (*L*), of about 250 c.c. capacity, the arc of shaking being about 20° and the frequency 200—220 per minute, giving effective break-up of the liquid surface with the formation of but little spray. The shaking vessel was contained in a water tank thermostatically controlled to 25° ± 0·05° c

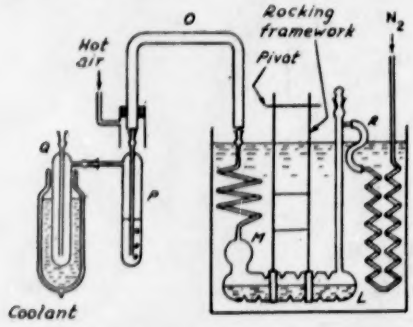


FIG. 1. *Saturator and condensers (not to scale).*

(see Fig. 1). It was shown experimentally that the calibration curve of the apparatus was not sensitive to small changes in temperature. During the shaking a stream of dry nitrogen, previously brought to the temperature of the thermostat, was swept over the mixture at rates of 40—60 c.c. per min., so that the time of contact of the gas stream with the mixture was about 3—4 min. It was shown also during one calibration experiment that an increase in the flow rate from 25 to 100 c.c. per min. did not produce a discontinuity in the curve and so did not affect the relative saturation of the vapour stream with trimethylamine and *cyclo*hexane. To prevent back diffusion while the carrier-gas stream was stopped during sampling, a clip was used to close the rubber tube (*R*).

After passage through a splash bulb (*M*) and the flexible spiral above it the gas stream from the saturator was conveyed through a side-arm (*O*), which was lagged and electrically heated to prevent premature condensation, into a double condenser. It was found that a small column of liquid, always less than 2 cm. in length, usually collected in the glass spiral in the course of an experiment. Although the heating coil or lagging of the side-arm could not be continued below the water level, it is thought unlikely that this was a result of premature condensation, since the quantity was not dependent on the rate of flow of gas nor did it depend upon the intensity of heating of the side-arm. The column of liquid probably resulted from spray.

In the first compartment of the double condenser (*P*) the gas stream bubbled through 6—10 c.c. of approximately 0·1N-hydrochloric acid, which removed the trimethylamine from it. The second compartment (*Q*) was cooled in acetone–solid carbon dioxide and the solvent was condensed in it. No odour of trimethylamine could be detected in the gas stream issuing from the condensers, but, in case trimethylamine passed into, and was frozen out in, the second, the contents of the two compartments were always mixed before the standard acid was titrated.

The weight fraction of trimethylamine in the condensate was determined by measuring the gain in weight of the condensers and determining the amount of standard acid neutralised during the condensation. A similar weighing and titration procedure was used in analysing the

reaction mixture, which was sampled with a pipette fitted with a rubber teat, at the beginning and the end of each distillation. The mean of the weight fractions found was taken for comparison with the weight fraction of trimethylamine in the condensate. Methyl-red was a satisfactory indicator, with a comparison flask, for these titrations, except when B was benzenethiol, in which case bromocresol-green was used as indicator in the analysis of the ternary solution. Because the total weight removed on analysis of the reaction mixture must be used in the calculation of successive values of y_b and all the sample cannot be transferred from the pipette to the flask containing standard acid, the length of the column of liquid remaining in the pipette was used as a measure of its weight in the application of a small correction.

(b) *Calorimetric measurements.* For the present work a precision of $\pm 5\%$ in the calorimetric determinations was deemed sufficient; so, since conservation of material was also desirable, the calorimeter was small. It consisted of a glass vessel with two legs. One, about 8·5 cm. long and 2·7 cm. in diameter, was the reaction compartment; this had a vacuum jacket and contained the hot junctions of the five-junction copper–constantan thermocouple. The other was a pocket for the cold junctions of the thermocouple, and contained *cyclo*hexane at the temperature of the thermostat bath in which the whole calorimeter was immersed. The temperature rise caused by reaction was observed; and when the temperature of the reaction compartment had again reached that of the bath, the electrical energy necessary to produce roughly the same rise in roughly the same time (*ca.* 25 sec.) was determined. The electrical heating coil was also used as a stirrer.

*cyclo*Hexane solutions containing 2—5% by weight of the reactants were used, and suitable amounts were weighed into the calorimeter from pipettes when required, both first being thermally equilibrated with the bath. The total volume of the mixed solutions was 2—3 c.c. From the initial concentrations of the two solutions, the quantities of each used, and the association constant K, the amount of complex formed could be calculated, and the heat of forming one mole of it thence derived.

Materials.—Nitrogen from a cylinder was used as carrier gas. It was dried by passage through concentrated sulphuric acid and then through a trap cooled in an acetone–solid carbon dioxide mixture.

Commercial *cyclo*hexane was purified by sulphonation and passage through a column of activated charcoal to remove aromatic impurities, followed by distillation from phosphoric oxide in a stream of dry air. Investigation of the range of temperature of freezing of the material showed that the content of impurity varied from 0·01 to 0·03 mole per 1000 g. of solvent, on the assumption that solid solutions were not formed on freezing. Aromatic impurities and thiophen were absent and the refractive index was reproducible to $\pm 5 \times 10^{-6}$. We believe that the impurities were methyl*cyclo*hexanes.

Two samples of trimethylamine were used. Both were prepared from the hydrochloride, made as described in *Organic Syntheses*, Coll. Vol. I, p. 514. The impure product of the first preparation was freed from unchanged ammonium chloride by recrystallisation from chloroform. The solution of trimethylamine in *cyclo*hexane was prepared by liberation of the compound from its salt by potassium hydroxide solution, passage of the gas over potassium hydroxide pellets to remove water, and liquefaction of the gas in a glass spiral cooled in dry ice. The liquid trimethylamine dropped into a flask containing dry *cyclo*hexane cooled in ice–water. This stock solution was used by two of us (J. A. P. and A. G.). In the course of the second preparation, it was observed that crystals of trimethylamine hydrochloric retain chloroform tenaciously, but may be freed from chloroform by recrystallisation from ethanol, though with considerable loss. A stock solution made as before from trimethylamine hydrochloride so purified was used by one of us (T. E. T.). It will be seen from the experimental results that the calibration curves of the apparatus with the two stock solutions differ slightly.

Commercial naphthalene, purified by recrystallisation twice from aqueous ethanol and dried *in vacuo* (P_2O_5), had m. p. 79·8° (cf. 80·10—80·27°; Timmermans, "Physico-chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950).

p-Nitrotoluene, recrystallised from ethanol and dried (H_2SO_4) *in vacuo*, had m. p. 51° (cf. 51·6—52·1°; Timmermans, *loc. cit.*).

p-Dichlorobenzene was purified by recrystallisation from ethanol and dried *in vacuo*; it had m. p. 53° (cf. 53·0—53·2°; Timmermans, *loc. cit.*).

Anisole was dried (P_2O_5) and distilled twice. It had b. p. 155° (cf. 153·75—153·9°; Timmermans, *loc. cit.*).

Phenol was distilled four times at atmospheric pressure and dried (P_2O_5) *in vacuo* for several days [m. p. 39·8—40·2° (cf. 40·7—41·0°; Timmermans, *loc. cit.*)].

p-Chlorophenol was fractionally distilled under reduced pressure (b. p. 106°/17 mm.) and

was dried (H_2SO_4) *in vacuo* [m. p. 42° (cf. 42·9°; Holleman and Rinkes, *Rec. Trav. chim.*, 1911, **30**, 83)].

o-Cresol was twice distilled at atmospheric pressure (b. p. 190°) and dried (P_2O_5) *in vacuo* for several days [m. p. 29·5—30° (cf. 30·35—30·94°; Timmermans, *loc. cit.*)].

m-Cresol was distilled at atmospheric pressure (b. p. 201—202°), followed by double fractional recrystallisation (m. p. 10·5—11·5°). It was then re-distilled [b. p. 201—201·5° (cf. b. p. 202·2—202·7°, m. p. 11·5—11·96°; Timmermans, *loc. cit.*)].

p-Cresol was distilled at atmospheric pressure (b. p. 195—197°) followed by double fractional recrystallisation and drying (P_2O_5) *in vacuo* for several days [m. p. 33—34° (cf. 34·4—34·6°; Timmermans, *loc. cit.*)].

Triphenylmethanol, recrystallised from carbon tetrachloride and dried at 90°, had m. p. 162·5° (cf. 164—165°; Stadnikow, *Ber.*, 1914, **47**, 2142).

n-Heptyl alcohol was shaken with successive lots of alkaline potassium permanganate solution until the solution was no longer decolorised after 15 min. It was then dried (K_2CO_3) and twice distilled at atmospheric pressure [b. p. 175—176° (cf. 175·6°; Butler, Thomson, and Maclennan, *J.*, 1933, 679)].

The 2 : 5-dimethylpyrrole used was prepared by Kofod, Sutton, and Jackson (*J.*, 1952, 1467). It was purified by redistillation under reduced pressure (b. p. 71°/19 mm.). Since it is rapidly oxidised in air the purified specimen was transferred direct from the receiver to the reaction mixture.

Indole was sublimed *in vacuo* [m. p. 52° (cf. 53°; Gluud, *Ber.*, 1915, **48**, 423)].

α- and β-Naphthol were recrystallised from boiling water and dried (P_2O_5) *in vacuo* for several days [m. p.s 95·5—96° and 122·5—123·5° respectively (cf. 94·2° and 121·6°; Kendall, *J. Amer. Chem. Soc.*, 1916, **38**, 1316).

Benzenethiol was distilled at atmospheric pressure [b. p. 168—168·5° (cf. 169·5°; Timmermans, *loc. cit.*)]. The purified specimen was used immediately.

Experimental Results

Equilibrium Constants.—The symbols used are as follows (see also p. 3891). Weight fractions: v_a, of trimethylamine in the condensate; y_a, of total trimethylamine in solution in terms of the whole solution; y_a', of total trimethylamine in solution, in terms of trimethylamine and *cyclo*hexane only [$y_a' = W_A/(W_A + W_B)$]; x_a, of free trimethylamine in solution, in terms of free trimethylamine and *cyclo*hexane only; y_b, of involatile reactant in solution. K is the association constant in moles/litre.

The results of two of us (J. A. P. and A. G.) should be considered separately from those of the third (T. E. T.) since slightly different experimental calibration curves were used. The results are contained in Tables 1 and 2.

Table 1. *Results at* 25°.

Calibration curves

No. 1 (J. A. P.)

$100v_a$	15·14	14·65	14·44	13·85	13·84	13·12	13·08	12·15	12·00	11·12	10·91	10·18
$100y_a$	0·768	0·735	0·728	0·693	0·684	0·636	0·627	0·586	0·595	0·545	0·545	0·500
$100v_a$	10·11	9·34	9·19	8·36	7·96	7·43	7·00	6·33	5·96	5·40	4·57	4·32
$100y_a$	0·498	0·453	0·448	0·404	0·384	0·357	0·328	0·301	0·279	0·254	0·218	0·203
$100v_a$	3·33	3·15	2·40	2·08	1·62	17·46	15·96	15·85				
$100y_a$	0·158	0·139	0·112	0·093	0·072	0·892	0·836	0·797				

No. 2 (A. G.)

$100v_a$	13·3	12·0	11·6	10·3	9·77	8·71	7·71	7·31	7·07	4·30	3·62	2·09
$100y_a$	0·641	0·598	0·553	0·505	0·459	0·416	0·374	0·336	0·289	0·201	0·162	0·105

The best smooth curve through the first set of points is given by:

$$100v_a = 22{\cdot}09\ (100y_a) - 2{\cdot}93\ (100y_a)^2$$

and the second set of points agrees well with this.

No. 3 (T. E. T.)

$100v_a$	12·91	12·61	12·41	11·78	11·22	10·84	10·61	9·74	9·01	8·78	7·93	7·79
$100y_a$	0·608	0·626	0·585	0·545	0·541	0·502	0·486	0·462	0·426	0·412	0·362	0·362
$100v_a$	7·07	6·52	6·01	5·22	4·22	2·45	2·45					
$100y_a$	0·318	0·302	0·274	0·245	0·194	0·154	0·114					

These points are linear and the best straight line is given by:

$$100v_a = 21{\cdot}38\ (100y_a) + 0{\cdot}04$$

TABLE 1. (*Continued.*)

Naphthalene (J. A. P.)

$100v_a$	15·05	13·81	12·76	11·59	10·41	9·25	8·07	6·92	5·74	4·58	3·21	1·98
$100y_a'$	0·762	0·702	0·640	0·583	0·515	0·450	0·388	0·326	0·269	0·209	0·149	0·095
$100x_a$	0·762	0·694	0·632	0·570	0·550	0·447	0·386	0·328	0·269	0·216	0·149	0·094

p-*Nitrotoluene* (J. A. P.)

$100v_a$	15·89	15·47	14·71	13·40	12·59	11·44	10·10	8·82	7·53	6·10	4·05	2·96
$100y_a$	0·826	0·802	0·765	0·689	0·643	0·585	0·509	0·437	0·371	0·295	0·196	0·141
$100y_a'$	0·852	0·827	0·786	0·711	0·663	0·599	0·525	0·451	0·382	0·306	0·202	0·148
$100x_a$	0·804	0·780	0·739	0·667	0·620	0·560	0·490	0·425	0·357	0·285	0·188	0·138
$100y_b$	2·959	2·961	2·976	2·983	2·998	3·019	3·036	3·060	3·088	3·124	3·182	3·248
K	0·37	0·37	0·41	0·40	0·42	0·46	0·43	0·36	0·42	0·37	0·47	0·30

p-*Dichlorobenzene* (J. A. P.)

$100v_a$	15·24	14·42	13·54	12·28	11·00	9·60	8·28	7·06	5·44	4·17	2·74
$100y_a$	0·785	0·737	0·682	0·612	0·542	0·467	0·401	0·340	0·258	0·196	0·127
$100x_a$	0·762	0·708	0·655	0·590	0·527	0·457	0·402	0·334	0·255	0·192	0·121
$100y_b$	2·982	2·995	3·010	3·024	3·045	3·070	3·097	3·124	3·161	3·210	3·271
K	0·41	0·48	0·48	0·45	0·39	0·34	0·19	0·30	0·27	0·32	0·55

Anisole (T. E. T.)

$100v_a$	18·23	16·73	15·48	14·74	13·75	12·62	11·68	11·22	9·98	9·20	8·12	7·49
$100y_a$	0·963	0·865	0·797	0·741	0·688	0·635	0·590	0·537	0·485	0·443	0·405	0·369
$100x_a$	0·944	0·855	0·782	0·739	0·684	0·623	0·572	0·548	0·483	0·442	0·387	0·357
$100y_b$	4·708	4·743	4·762	4·779	4·799	4·818	4·836	4·857	4·883	4·908	4·933	4·960
K	0·21	0·18	0·22	0·16	0·17	0·21	0·24	0·09	0·16	0·15	0·29	0·25

Phenol (J. A. P.)

$100v_a$	16·38	15·85	14·68	13·50	12·70	11·78	10·85	9·42	8·30	8·03	7·25	6·32
$100y_a$	1·258	1·226	1·159	1·091	1·050	0·992	0·936	0·857	0·793	0·777	0·731	0·679
$100y_a'$	1·264	1·235	1·168	1·099	1·052	1·000	0·945	0·864	0·799	0·783	0·738	0·684
$100x_a$	0·835	0·806	0·733	0·670	0·635	0·578	0·529	0·462	0·403	0·390	0·348	0·303
$100y_b$	0·751	0·756	0·756	0·758	0·766	0·766	0·774	0·776	0·787	0·757	0·767	0·769
K	102	90	108	102	87	93	82	78	76	93	87	91
$100v_a$	5·54	4·77	4·05									
$100y_a$	0·634	0·582	0·535									
$100y_a'$	0·639	0·586	0·541									
$100x_a$	0·267	0·223	0·183									
$100y_b$	0·776	0·784	0·793									
K	107	95	103									

Phenol (A. G.)

$100v_a$	16·70	15·08	12·90	11·76	10·60	9·61	8·48	7·36	6·35	5·83	4·82	2·50
$100y_a$	1·371	1·268	1·120	1·055	0·995	0·928	0·856	0·797	0·750	0·695	0·625	0·469
$100x_a$	0·855	0·758	0·635	0·574	0·515	0·465	0·407	0·353	0·311	0·275	0·225	0·110
$100y_b$	0·857	0·863	0·868	0·873	0·882	0·888	0·896	0·904	0·907	0·916	0·928	0·983
K	324	175	100	94	97	81	72	78	81	75	72	96
$100v_a$	1·50	1·03										
$100y_a$	0·398	0·341										
$100x_a$	0·069	0·045										
$100y_b$	1·03	1·09										
K	111	127										

Phenol (T. E. T.)

$100v_a$	10·28	9·75	8·92	8·44	7·46	6·59	5·87	5·17	4·38	3·68
$100y_a$	0·959	0·917	0·878	0·839	0·791	0·740	0·708	0·665	0·611	0·569
$100x_a$	0·498	0·471	0·428	0·404	0·355	0·311	0·277	0·242	0·203	0·171
$100y_b$	0·841	0·845	0·849	0·854	0·859	0·866	0·873	0·881	0·891	0·903
K	118	93	105	86	96	96	106	107	103	108

Phenol (T. E. T.)

$100v_a$	2·38	2·25	2·02	1·76	1·67	1·53	1·35	1·18	1·04	0·86
$100y_a$	0·497	0·489	0·473	0·451	0·435	0·420	0·405	0·391	0·376	0·359
$100x_a$	0·109	0·103	0·093	0·080	0·076	0·070	0·061	0·053	0·047	0·038
$100y_b$	1·024	1·031	1·041	1·052	1·065	1·080	1·096	1·115	1·138	1·171
K	108	111	115	124	118	118	126	136	140	156

p-*Chlorophenol* (J. A. P.)

$100v_a$	9·50	8·87	8·18	7·06	6·67	4·42	3·46	2·36
$100y_a$	0·893	0·859	0·794	0·757	0·678	0·609	0·553	0·492
$100x_a$	0·459	0·427	0·373	0·338	0·269	0·206	0·162	0·105
$100y_b$	1·007	1·006	1·014	1·024	1·038	1·050	1·069	1·095
K	350	330	228	205	186	201	193	246

TABLE 1. (*Continued.*)

p-*Cresol* (J. A. P.)

$100v_a$	11·35	9·40	8·79	7·63	6·35	5·19	3·98	3·05
$100y_a$	0·895	0·842	0·810	0·741	0·667	0·601	0·533	0·481
$100x_a$	0·500	0·453	0·424	0·366	0·301	0·244	0·185	0·139
$100y_b$	0·906	0·906	0·915	0·924	0·932	0·947	0·962	0·983
K	63	65	67	64	69	72	82	99

p-*Cresol* (T. E. T.)

$100v_a$	12·04	11·26	10·12	9·18	8·17	7·18	6·12	5·11	4·04	3·15
$100y_a$	0·898	0·835	0·794	0·746	0·691	0·633	0·560	0·505	0·464	0·400
$100x_a$	0·561	0·525	0·472	0·428	0·380	0·334	0·284	0·237	0·187	0·146
$100y_b$	0·718	0·721	0·725	0·729	0·734	0·740	0·746	0·754	0·764	0·777
K	96	59	77	77	73	69	59	62	83	75

o-*Cresol* (T. E. T.)

$100v_a$	2·68	2·48	2·29	2·14	1·96	1·79	1·65	1·36	1·28
$100y_a$	0·567	0·552	0·534	0·520	0·508	0·495	0·475	0·458	0·439
$100x_a$	0·124	0·114	0·105	0·098	0·090	0·082	0·075	0·062	0·058
$100y_b$	1·504	1·513	1·525	1·538	1·553	1·569	1·589	1·617	1·635
K	73	83	79	81	84	88	88	101	97

o-*Cresol* (T. E. T.)

$100v_a$	5·74	5·24	4·58	4·10	3·59	3·04	2·51	
$100y_a$	0·660	0·622	0·583	0·547	0·510	0·476	0·439	
$100x_a$	0·267	0·243	0·212	0·190	0·166	0·140	0·116	
$100y_b$	1·008	1·015	1·023	1·032	1·043	1·056	1·073	
K	74	70	73	71	71	78	73	

m-*Cresol* (T. E. T.)

$100v_a$	10·25	9·24	8·17	6·95	6·39	5·38	4·45	3·43	2·74
$100y_a$	0·846	0·789	0·735	0·692	0·635	0·574	0·519	0·475	0·419
$100x_a$	0·478	0·430	0·380	0·323	0·297	0·250	0·206	0·159	0·126
$100y_b$	0·823	0·828	0·833	0·829	0·846	0·856	0·867	0·881	0·900
K	79	74	77	103	73	71	74	94	91

Triphenylmethanol (T. E. T.)

$100v_a$	12·60	11·35	10·19	9·86	8·82	8·08	7·17	6·50	5·88	5·30
$100y_a$	0·753	0·677	0·635	0·591	0·534	0·480	0·435	0·393	0·360	0·321
$100x_a$	0·621	0·554	0·493	0·476	0·423	0·386	0·340	0·307	0·277	0·247
$100y_b$	1·140	1·145	1·151	1·157	1·164	1·172	1·178	1·184	1·192	1·200
K	14·5	13·7	20·4	13·9	14·3	11·8	13·5	12·5	13·2	12·2

Triphenylmethanol (T. E. T.)

$100v_a$	16·67	15·83	14·26	13·16	11·98	10·78	9·94	9·17	8·26	7·47	6·73
$100y_a$	0·930	0·850	0·778	0·710	0·652	0·602	0·552	0·503	0·454	0·410	0·372
$100x_a$	0·850	0·802	0·713	0·652	0·589	0·524	0·480	0·440	0·394	0·365	0·317
$100y_b$	0·859	0·863	0·867	0·872	0·877	0·882	0·887	0·892	0·898	0·903	0·909
K	7·4	3·8	6·1	5·6	6·9	10·3	9·9	8·6	8·8	8·6	9·4

Triphenylmethanol (T. E. T.)

$100v_a$	8·14	7·15	6·46	5·67	4·80	4·21	3·51	2·92	2·41	1·92
$100y_a$	0·420	0·382	0·340	0·300	0·263	0·226	0·193	0·163	0·130	0·105
$100x_a$	0·370	0·333	0·300	0·263	0·223	0·195	0·162	0·135	0·111	0·088
$100y_b$	0·574	0·576	0·580	0·585	0·590	0·595	0·601	0·607	0·614	0·623
K	10·1	14·4	11·8	12·0	15·0	12·3	14·3	15·0	11·4	12·5

n-*Heptyl alcohol* (T. E. T.)

$100v_a$	8·72	8·10	7·35	6·75	6·30	5·81	5·05	4·68	4·28	3·89	3·55
$100y_a$	0·535	0·496	0·463	0·429	0·396	0·356	0·325	0·300	0·268	0·240	0·214
$100x_a$	0·418	0·386	0·348	0·319	0·297	0·273	0·236	0·218	0·198	0·181	0·164
$100y_b$	2·076	2·086	2·096	2·108	2·120	2·134	2·148	2·162	2·179	2·198	2·217
K	2·5	2·7	2·9	3·0	2·8	2·5	3·1	3·1	2·8	2·6	2·4

n-*Heptyl alcohol* (T. E. T.)

$100v_a$	9·25	9·03	8·21	7·64	7·06	6·57	6·24	5·29	4·69	4·16
$100y_a$	0·531	0·493	0·461	0·428	0·386	0·347	0·320	0·285	0·263	0·227
$100x_a$	0·406	0·395	0·355	0·327	0·300	0·278	0·265	0·221	0·194	0·171
$100y_b$	1·134	1·139	1·143	1·149	1·154	1·160	1·166	1·173	1·182	1·191
K	5·5	4·2	5·1	5·1	4·6	3·8	3·2	4·4	5·3	4·8

TABLE 1. (*Continued.*)

n-Heptyl alcohol (T. E. T.)

$100v_a$	7·53	7·06	6·57	5·60	5·26	4·77	4·32	3·63	3·18	2·67
$100y_a$	0·417	0·386	0·368	0·337	0·306	0·274	0·244	0·215	0·188	0·159
$100x_a$	0·350	0·328	0·305	0·265	0·244	0·221	0·200	0·168	0·147	0·123
$100y_b$	1·046	1·050	1·055	1·060	1·067	1·073	1·081	1·090	1·099	1·110
K	3·4	3·0	3·5	4·7	4·3	3·9	3·5	4·4	4·3	4·4

2 : 5-*Dimethylpyrrole* (T. E. T.)

$100y_a$	7·18	6·78	6·45	5·89	5·56	5·17	5·00	4·59	4·18	3·70
$100y_a$	0·395	0·380	0·352	0·332	0·313	0·296	0·283	0·259	0·236	0·213
$100x_a$	0·305	0·289	0·273	0·249	0·234	0·215	0·208	0·190	0·171	0·152
$100y_b$	1·184	1·188	1·192	1·197	1·202	1·206	1·210	1·216	1·223	1·232
K	3·7	3·9	3·5	4·0	4·0	4·5	4·3	4·2	4·3	4·5

Indole (T. E. T.)

$100y_a$	15·21	14·33	12·98	12·15	11·01	9·71	8·62	7·31	5·95	4·63	3·33
$100y_a$	0·913	0·843	0·766	0·715	0·653	0·583	0·513	0·436	0·358	0·277	0·209
$100x_a$	0·710	0·668	0·605	0·566	0·513	0·452	0·401	0·340	0·276	0·215	0·154
$100y_b$	0·631	0·634	0·637	0·641	0·645	0·649	0·655	0·662	0·670	0·681	0·694
K	20·3	14·8	13·4	12·3	11·9	11·9	10·2	9·4	9·2	8·1	9·5

α-*Naphthol* (T. E. T.)

$100v_a$	6·59	6·10	5·65	5·28	4·88	4·22	3·88	3·36	3·00	2·50
$100y_a$	0·434	0·415	0·398	0·375	0·352	0·332	0·311	0·286	0·263	0·244
$100x_a$	0·306	0·283	0·262	0·245	0·226	0·196	0·180	0·155	0·138	0·115
$100y_b$	0·398	0·399	0·400	0·401	0·404	0·406	0·408	0·411	0·415	0·418
K	96	119	150	123	113	184	160	179	155	204

α-*Naphthol* (T. E. T.)

$100v_a$	8·40	7·72	6·88	6·60	5·74	5·04	4·54	3·85
$100y_a$	0·509	0·482	0·455	0·425	0·393	0·363	0·335	0·303
$100x_a$	0·391	0·359	0·320	0·307	0·267	0·234	0·211	0·178
$100y_b$	0·359	0·360	0·362	0·364	0·364	0·368	0·370	0·373
K	84	114	272	100	166	208	171	203

β-*Naphthol* (T. E. T.)

$100v_a$	12·29	11·36	10·61	9·62	9·00	8·11	7·17	6·76	5·90
$100y_a$	0·645	0·612	0·580	0·541	0·500	0·462	0·429	0·395	0·357
$100x_a$	0·573	0·530	0·494	0·448	0·419	0·378	0·334	0·314	0·274
$100y_b$	0·222	0·222	0·223	0·224	0·225	0·226	0·227	0·228	0·230
K	580	1650	3740	—	1430	2190	—	1670	2230

β-*Naphthol* (T. E. T.)

$100v_a$	8·44	7·73	7·07	6·55	5·64	5·02	4·56	3·81	3·12
$100y_a$	0·513	0·475	0·445	0·410	0·374	0·340	0·305	0·277	0·249
$100x_a$	0·393	0·360	0·329	0·305	0·262	0·233	0·211	0·176	0·144
$100y_b$	0·297	0·299	0·300	0·302	0·303	0·306	0·308	0·311	0·314
K	8200	423	502	156	307	199	109	171	243

Benzenethiol (T. E. T.)

$100v_a$	9·08	8·65	7·75	7·08	6·53	5·82	5·02	3·65
$100y_a$	0·431	0·396	0·360	0·329	0·302	0·273	0·237	0·167
$100x_a$	0·423	0·402	0·361	0·329	0·304	0·207	0·232	0·168
$100y_b$	1·867	1·874	1·882	1·890	1·898	1·909	1·921	1·949
K	0·33	0·04	0·13	0·14	0·10	0·24	0·34	0·09

Calorimetric Measurements.—Phenol. Three separate determinations were made with a 3·7% (by wt.) phenol solution and a 4·9% (by wt.) trimethylamine solution. The three values of the molar heat of formation of the complex were 5·6, 5·9, and 5·5 kcal., leading to a mean heat of formation of the phenol–trimethylamine complex of 5·7 ± 0·2 kcal./mole.

p-*Chlorophenol.* Two separate determinations were made, at a *p*-chlorophenol concentration of 2·7% (by wt.) and a trimethylamine concentration of 4·9%. The two heats of formation were 7·4 and 8·6 kcal./mole, and it is therefore concluded that the heat of formation of the *p*-chlorophenol–trimethylamine complex is 8·0 ± 0·6 kcal./mole.

TABLE 2. *Results at* 43·7°.

Calibration curve (A. G.)

$100v_a$	14·85	13·65	13·10	12·30	11·56	10·30	8·53	7·08	5·39	3·44	2·53
$100y_a$	1·032	0·928	0·871	0·810	0·736	0·655	0·527	0·447	0·342	0·218	0·168

Phenol (A. G.)

$100v_a$	6·11	4·93	3·85	3·01
$100y_a$	0·825	0·717	0·628	0·554
$100x_a$	0·390	0·315	0·245	0·190
$100y_b$	0·963	0·986	1·010	1·044
K	50	45	47	49

p-*Chlorophenol* (A. G.)

$100v_a$	9·83	7·98	6·71	5·25	4·14	2·77
$100y_a$	0·995	0·886	0·782	0·688	0·603	0·524
$100x_a$	0·622	0·505	0·423	0·335	0·262	0·175
$100y_b$	0·908	0·919	0·933	0·948	0·967	0·993
K	114	157	92	108	97	138

p-*Cresol* (A. G.)

$100v_a$	6·57	5·39	4·45	3·68	2·94	2·12
$100y_a$	0·747	0·650	0·566	0·500	0·434	0·366
$100x_a$	0·415	0·340	0·282	0·235	0·198	0·132
$100y_b$	0·833	0·847	0·865	0·883	0·908	0·941
K	47	44	40	40	41	46

DISCUSSION

The first requirement for the present method to be satisfactory is that an inert second solute shall not change the relation between the A : S ratios in the vapour and liquid phases. That this is so is demonstrated by the results with B = naphthalene, shown in Fig. 2, in which the abscissa used is not $y_a = W_A/W$, but $y_a' = W_A/(W - W_B)$; if no complex is formed, and if there is no deviation from the simple theory, the experimental points will then lie directly on the calibration curve, as indeed they do.

If we use as B a substance which would not be expected to form hydrogen bonds but which, because it is dipolar, might cause a deviation from the simple theory, we find that the points do not now fall on the calibration curve but somewhat below it. Thus Fig. 2 shows that *p*-nitrotoluene has this effect; and the tabulated results show that *p*-dichlorobenzene and anisole have it too. In order to give these results some quantitative expression we may treat them as being due to the formation of a 1 : 1 complex, when we find for K values of 0·4, 0·35, and 0·2, in mole/l. units, respectively.

If, now, B is phenol which would be expected to form a hydrogen-bonded, 1 : 1 complex with trimethylamine, the experimental points show a marked departure from the calibration curve (Fig. 2) and an association constant can be calculated from each one. Series of such values obtained by three of the authors independently are plotted in Fig. 3. There is a considerable scatter of points between 60 and 100 for K, and, further, the curve of the points of any one run shows a minimum. The errors of precision between different experiments are about 20%, probably due to slight differences in starting conditions and particularly in the purity of the solvent, but the variation of K over a single experiment is too great to be explained by any obvious precision errors occurring therein. The K values lie on smooth curves in most of the systems wherein hydrogen bonding is indicated, although these curves do not always display minima. There is usually a rise at low concentrations.

If K is really constant, we can readily see that an anomalous increase in K corresponds to the trimethylamine's being less available in the ternary solution than it should be, relative to its availability in the binary amine–solvent mixture. This might be due to some kind of systematic error; but careful consideration of the possibilities has not revealed one. Because of the difficulty of fixing the starting conditions, it is not practicable to repeat the points obtained in the later stages of a previous run as the first points in a subsequent run, *i.e.*, the obvious tests of reproducibility are not easy to apply.

The next possibility considered was that the anomalies arise from over-simplification in the theory. The assumption that only short-range, specific forces need be considered is not quite correct, as the results with *p*-nitrotoluene, *p*-dichlorobenzene, and anisole show.

Therefore attempts were made to allow for inter-dipolar forces between the trimethylamine and the phenol, and also between it and the polar, hydrogen-bonded complex. From the results for the above three compounds in relation to their total *scalar* dipole moments (4·4, 3·1, and 1·28 D, respectively) it is possible to assess roughly the K values for these two interactions, with phenol ($\mu = 1{\cdot}54$ D, see Hulett, Pegg, and Sutton, following paper) and with the complex ($\mu = 3{\cdot}24$ D, *idem, ibid.*). Another correction is needed for the self-association of phenol. This was attempted by using the constant for dimerisation in carbon tetrachloride calculated from Fox and Martin's results (*Proc. Roy. Soc.*, 1937, *A*, **162**, 419). These calculations, which are equivalent to trying to obtain activity coefficients for the two reactants, though but approximate, suffice to show that these causes are quite inadequate to account for the variation in K. It is indeed difficult to see how any explanation based on activities can explain an anomaly which increases as infinite dilution is approached.

FIG. 2. *The effect of naphthalene* (○), *p-nitrotoluene* (●), *and phenol* (×) *on the vapour-phase concentration of trimethylamine. The calibration curve is shown as a solid line.*

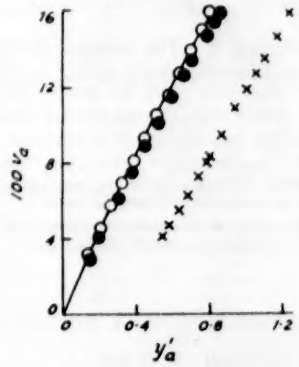
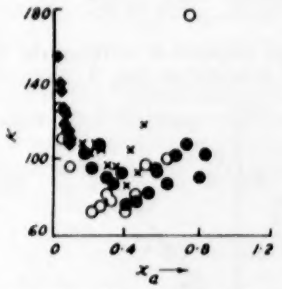


FIG. 3. *The variation of K for phenol–trimethylamine between runs, and with concentration.*



● *Run no.* 1; ○ *run no.* 2; × *run no.* 3; ◆ *run no.* 4.

Another possible cause is that the complexes are not simply 1 : 1 (Davies, *Ann. Reports*, 1946, **43**, 5; McDougall, *J. Amer. Chem. Soc.*, 1941, **63**, 3420): this seems unconvincing because the anomaly for indole–trimethylamine is similar. Yet another is that there is not merely one kind of 1 : 1 complex but an infinite variety because the forces between the amine nitrogen atom and the acidic hydrogen atom are relatively long range, so that the treatment by a single equilibrium is inadequate. These possibilities have been considered in greater detail, but attempts to treat them rigorously were unsatisfactory.

We have therefore been forced to the conclusion that the variations may be real, and that we cannot at present explain them satisfactorily. Because of the possibility that values outside the range of those now observed might be obtained under different conditions, the quantitative significance of the K values is uncertain. Nevertheless the minimum values of K appear to be characteristic of particular associations (Fig. 3) and appear at least to be qualitatively useful and informative because the range thereof is so very large. In the rest of the discussion, comparisons will be made between them.

The best values of K thus obtained are shown in Table 3.

From Fig. 4, in which the logarithms of the dissociation constants in water (k) * and of the association constants with trimethylamine in *cyclo*hexane (K) are plotted against each other, it is clear, despite all the uncertainties, that the more acidic a compound is in water the stronger in general is the complex which it forms with the amine in a non-polar solvent. This is to be expected on the electrostatic theory of hydrogen-bond formation if there is also a parallel between the electric dipole moment of the X–H bond and the acid

* k_{water} for *p*-chlorophenol is taken, by analogy with the values for *p*-fluorophenol, to be four times the value in 30% ethanol–water (Bennett, Brooks, and Glasstone, *J.*, 1935, 1821).

TABLE 3.

B	K (mole fraction units)	K (mole/l. units)	Type of bonding
	At 25°		
Naphthalene	0	0	Nil
p-Nitrotoluene	3·5 ± 1	0·4	Dipole–dipole
p-Dichlorobenzene	2·7 ± 1	0·35	,,
Anisole	1·8 ± 1	0·2	,,
Benzenethiol	2·5 ± 1	0·3	,,
Phenol	800 ± 200	86	Hydrogen bonding
o-Cresol	650 ± 150	70	,,
m-Cresol	650 ± 150	70	,,
p-Cresol	600 ± 150	65	,,
p-Chlorophenol	1700 ± 300	200	,,
α-Naphthol	1000 ± 200	110	,,
β-Naphthol	2100 ± 400	230	,,
Triphenylmethanol	110 ± 20	12	,,
n-Heptyl alcohol	32 ± 8	3·5	,,
2 : 5-Dimethylpyrrole	32 ± 8	3·5	,,
Indole	85 ± 15	9	,,
	At 43·7°		
Phenol	430	46	—
p-Chlorophenol	720	76	—
p-Cresol	380	40	—

dissociation constant in water of the molecule containing it. The compounds, triphenylmethanol, *n*-heptyl alcohol, 2 : 5-dimethylpyrrole, and indole, which do not appear in this

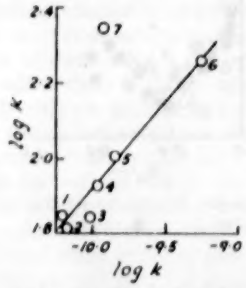


FIG. 4. *The relation between association constant K and electrolytic dissociation constant in water k.*

1, o-*Cresol*; 2, p-*cresol*; 3, m-*cresol*; 4, *phenol*; 5, α-*naphthol*; 6, p-*chlorophenol*; 7, β-*naphthol*.

graph because their acid dissociation constants are small and not easily measurable, form complexes which are much less stable than those with the phenols but which nevertheless are distinct from those formed by polar molecules without acidic hydrogen atoms.

There are two exceptions to this rule. Benzenethiol forms a very much less stable complex than would be expected: it is no stronger than a so-called dipole–dipole complex. By comparison with anisole the electric dipole moment of benzenethiol (1·33 D) should give a K value of about 0·2, while the actual value is 0·3. Gordy and Stanford (*J. Amer. Chem. Soc.*, 1940, **62**, 497) conclude that, in benzene solution, benzenethiol does not associate and that complex formation does not occur between thiophenol and amines less basic than pyridine, while with tripentylamine there seems to be salt formation. Trimethylamine probably has an intermediate basicity, so on this evidence a hydrogen-bonded complex might be expected. Copley, Marvel, and Ginsberg (*J. Amer. Chem. Soc.*, 1939, **61**, 3161) interpreted anomalous heats of mixing of some oxygen and some nitrogen compounds with benzenethiol as evidence of hydrogen-bond formation, though these were less than those when the same compounds were mixed with phenylacetylene and much less than those with chloroform. The experiments were, however, carried out at much higher concentrations than were ours.

The apparent paradox between this result for benzenethiol and its acid dissociation constant relative to that of phenol needs some consideration. An empirical explanation is provided by Schwarzenbach's observation that its dissociation constant is much more sensitive to the dielectric constant of the solvent than is that of phenol. He found (*Helv. Chim. Acta*, 1932, **15**, 1468) that in 60% ethanol–water, k for benzenethiol is $2{\cdot}31 \times 10^{-10}$

while in water (by extrapolation) it is $2{\cdot}89 \times 10^{-7}$; this is an increase of a thousandfold, whereas for phenol the increase is only about sixfold. The stability of the benzenethiol–trimethylamine complex will depend essentially upon the polar character of the X–H bond, and it is likely that this is considerably less in S–H than in O–H, at least in a medium of low dielectric constant. The moment of benzenethiol might arise largely from unshared electrons on the sulphur atom.

The second exception is the anomalous stability of the β-naphthol complex, which might be due to the greater heat of formation of the hydrogen bond, or to the partial screening of the α-hydroxyl group by the *peri*-hydrogen atom on the second ring. This matter is more appropriately discussed in the following paper which deals with the electric dipole moment changes.

From the results for K at 25° and 43·7° for three phenols, it is possible to calculate ΔH, and thence, from the ΔF values given by the association constants, rough values of ΔS can be derived. The results of the calorimetric measurements are given in Table 5 for comparison: these, of course, require a knowledge of K values for their evaluation.

TABLE 5.

Compound	ΔF (kcal./mole)	ΔH (kcal./mole) Thermodynamic	Calorimetric	ΔS (cal./mole/°c)
Phenol	−2·6	−5·8	−5·7	−10
p-Chlorophenol	−3·1	−7·0	−8·0	−13
p-Cresol	−2·4	−3·8	—	− 5

The values are all quite rough, but the agreement of the " thermodynamic " and the calorimetric values for ΔH, and the general reasonableness of the results support the view that the method of investigating equilibria described herein gives association constants of more than qualitative significance. The wider significance of these ΔH values will be considered in the following paper.

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The Electric Dipole Moments of Some Hydrogen-bonded Complexes.

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Measurements have been made of the changes of electric dipole moment ($\Delta\mu$) which occur when trimethylamine forms complexes with weakly acidic substances in *cyclo*hexane solution. The change is about 1·0 D for the amine with phenol, the positive pole being on the nitrogen atom. This indicates a contribution of not more than 10% from the structure $O^- H{-}N^+\leqslant$, which is roughly what might be expected from the electronegativities of the atoms, and which confirms that the hydrogen-bond proper is largely ionic. For *p*-cresol the change is less (0·9 D), while for *p*-chlorophenol it is greater (1·26 D); so these moment changes, the $-\Delta H$ values (preceding paper), and the acid dissociation constants in water all increase together, and presumably are due to increase of the O–H bond moment in this order.

In general there is fairly good proportionality between $(\Delta\mu)^2$ and K, the association constant for the complex; this confirms the observation previously reported that the association constant is greater for β-naphthol than for α-naphthol although the acid dissociation constant in water is smaller.

IN the preceding paper, approximate values were reported for the association constants, K, for complex formation in *cyclo*hexane solution between trimethylamine and various substances containing a more or less acidic hydrogen atom. In this paper, these are combined with electric polarisation values to give the dipole moments of the complexes. The significance of the values so obtained is considered.

Experimental

Method of expressing and of using the Polarisation Results.—Suppose the initial solution contains a moles of trimethylamine, b of the "acidic" substance, and s of *cyclo*hexane. If, after reaction has taken place, x moles of the 1 : 1 complex are formed, the total number of moles in solution is s of *cyclo*hexane, $a - x$ of trimethylamine, $b - x$ of acidic component, and x of complex, *i.e.*, a total of $a + b + s - x$.

From these, the respective molar fractions of each substance may be obtained. If we assume that molar fractions can be taken as the active masses of each reactant, which is not exactly true but is sufficiently so for our purposes (see preceding paper), the mass action equilibrium constant K is given by

$$K = \frac{x}{(a - x)(b - x)} \times (a + b + s - x)$$

By arranging this as a quadratic equation in x, and, bearing in mind the uncertainties in the K values as obtained in the previous paper, we may assume, K being of the order 75 to 2000 when so expressed, that $K + 1 \approx K$, whence

$$x = [K(a + b) + s - \{[K(a + b) + s]^2 - 4Kab\}^{\frac{1}{2}}]/2K$$

Using the values of x so derived, we may obtain the weight fractions of each molecular species present at equilibrium. Let these be denoted by w_1, w_2, w_3, and w_4 for *cyclo*hexane, trimethylamine, acidic component, and complex, respectively. We may write the total specific polarisation ${}_T p$ (that is, the sum of the distortion and the orientation polarisations) for the solution as

$${}_T p = (\varepsilon - 1)v/(\varepsilon + 2) = w_1 {}_T p_1 + w_2 {}_T p_2 + w_3 {}_T p_3 + w_4 {}_T p_4$$

where ε is the observed dielectric constant for the solution and v the specific volume. ${}_T p_1$, etc., represent the total specific polarisations for each component. ${}_T p_1$ is obtained, as $v_1(\varepsilon_1 - 1)/(\varepsilon_1 + 2)$, by direct observations on the solvent. ${}_T p_2$ is taken to be 0·5994 c.c. from work by Le Fèvre (*Trans. Faraday Soc.*, **1947**, **43**, 374). ${}_T p_3$ can be obtained from the literature, but for phenol and for triphenylmethanol it has been redetermined. Hence, ${}_T p_4$ can be calculated and thence the total *molar* polarisation ${}_T P_4 = (M_2 + M_3) {}_T p_4$, where M_2 is the molecular weight of species whose weight fraction is w_2, etc. The molar electron polarisation of the complex may be taken as the sum of those for its constituents, *i.e.*, ${}_E P_4 = {}_E P_2 + {}_E P_3$ which are available in the literature. Thus, the molar orientation polarisation, ${}_O P_4$, for the complex is obtained as ${}_T P_4 - {}_E P_4$, and so the moment of the complex as $\mu = 0{\cdot}2212({}_O P_4)^{\frac{1}{2}}$.

The moments obtained for each of three or four separate solutions are averaged. The errors quoted are obtained by considering the scatter of these values, on the assumption that the K value is definitive, and therefore they reflect only the uncertainties of the polarisation measurements.

As already mentioned, the electric dipole moments of phenol and of triphenylmethanol were also measured to check existing data. The dielectric constants, ε, specific volumes, v, and the differences of the refractive indices from that of the pure solvent, Δn, were measured for a series of benzene solutions containing various weight fractions, w, of the solute; and they were used for calculating the moments in the usual way (see Everard, Hill, and Sutton, *Trans. Faraday Soc.*, **1950**, **46**, 417). The molar electron polarisations were also calculated, as ${}_E P = 10^{-6} M(29{,}312\beta + 57{,}145\gamma + 33{,}566)$, β and γ being the gradients of the v–w, and the n–w plots, respectively.

Apparatus and Techniques.—The dielectric constants were measured by means of the apparatus and technique described by Hill and Sutton (*J.*, 1953, 1482). Specific volumes were measured by means of a Sprengel–Ostwald type pyknometer. Refractive index differences were measured on a Pulfrich refractometer.

Solutions were made up as follows. The solid solute was weighed into a conical flask having a well-fitting ground-glass stopper. The *cyclo*hexane was added to this and the flask re-weighed. When solution was complete, about 2 ml. of a 5% solution of trimethylamine in *cyclo*hexane were added, and the flask again weighed. The mixture was transferred to the dielectric cell by replacing the stopper by a cork bearing an inverted U-tube and a short capillary connected to the dry air supply. The concentration of trimethylamine was back-titrated acidimetrically in a weighed amount of solution taken from the dielectric cell immediately after measurement.

Purification of Materials.—*cyclo*Hexane was purified as described in the preceding paper

save that the passage through activated charcoal was omitted, and instead it was subjected to two successive fractional freezing processes in which the residual one-sixth was rejected each time.

Benzene (" AnalaR ") was purified by triple fractional freezing.

Both *cyclo*hexane and benzene were dried (P_2O_5), and were then distilled from fresh pentoxide in a stream of dry air.

p-*Fluorophenol.* A specimen supplied by Imperial Chemical Industries Limited was distilled in an all-glass apparatus, the fraction of b. p. 184·5—186° being collected. This was crystallised and was stored in a desiccator (P_2O_5) until required [m. p. 48·3° (cf. 48·2°, Swartz, *J. Chim. phys.*, 1919, **17**, 26)].

Other materials were purified as described in the preceding paper. The results are shown in Tables 1 and 2.

TABLE 1. *Electric dipole moments of individual compounds in benzene.*

Phenol

w	ε	v	Δn
0·002483	2·27733	1·14438	0·000209
0·004138	2·28315	1·14388	0·000223
0·006288	2·28912	1·14340	0·000327
0·007794	2·29344	1·14305	0·000404
0·008535	2·29494	1·14292	0·000494
0·010432	2·30046	1·14246	0·000523
0·014840	2·31449	1·14132	0·000784

Whence, $\varepsilon = 2{\cdot}2710 + 2{\cdot}84\,w$; $v = 1{\cdot}14485 - 0{\cdot}228\,w$; $n = 0{\cdot}000018 + 0{\cdot}0483\,w$

${}_0P = 48{\cdot}09$ c.c.; ${}_\infty P = 27{\cdot}90$ c.c.; $\mu = 1{\cdot}53(4)$ D.

Triphenylmethanol

w	ε	v	Δn
0·002602	2·2763	1·14411	0·000135
0·004111	2·2785	1·14383	0·000412
0·006121	2·2809	1·14317	0·000602
0·001737	2·2755	—	0·000105

Whence, $\varepsilon = 2{\cdot}2732 + 1{\cdot}240\,w$; $v = 1{\cdot}14493 - 0{\cdot}286\,w$; $n = 0{\cdot}000118 + 0{\cdot}1176\,w$

${}_0P = 43{\cdot}93$ c.c.; ${}_\infty P = 83{\cdot}05$ c.c.; $\mu = 1{\cdot}46(6)$ D.

Smyth and Dornte reported a value of 2·11 (*J. Amer. Chem. Soc.*, 1931, **53**, 546); recalculation from their observations gives 1·64 D.

TABLE 2. *Electric dipole moments of complexes.*

s	a	b	ε	v	x	${}_TP_4$
			Phenol–trimethylamine complex			
0·44677	0·001606	0·002278	2·0479	1·2836	0·001098	260·3
0·46904	0·003662	0·004328	2·0851	1·2826	0·002577	262·1
0·48080	0·001797	0·002010	2·0449	1·2840	0·001088	267·6
	*cyclo*Hexane	—	2·0139	1·2849	—	—

$K = 800 \pm 200$; ${}_Tp_3 = 0{\cdot}8081$ c.c.; ${}_\infty P_3 = 27{\cdot}90$ c.c.
Hence, average ${}_TP_4 = 263{\cdot}3$ c.c.; $\mu = 3{\cdot}24 \pm 0{\cdot}03$ D.

			p-*Cresol–trimethylamine complex*			
0·474971	0·001661	0·002108	2·0146	1·2837	0·000977	244·6
0·472827	0·001725	0·003303	2·0556	1·2827	0·001247	270·0
0·521781	0·002222	0·003711	2·0578	1·2826	0·001578	259·3
	*cyclo*Hexane	—	2·0141	1·2848	—	—
0·450732	0·001778	0·002275	2·0472	1·2835	0·001089	256·4
0·442700	0·001596	0·001383	2·0347	1·2842	0·000742	234·7
0·482380	0·001477	0·002080	2·0399	1·2838	0·000884	250·7
	*cyclo*Hexane	—	2·0141	1·2849	—	—

$K = 600 \pm 200$; ${}_Tp_3 = 0{\cdot}7571$; * ${}_\infty P_3 = 31{\cdot}3$ c.c.*
Hence, average ${}_TP_4 = 252{\cdot}6$ c.c.; $\mu = 3{\cdot}13 \pm 0{\cdot}06$ D.

			o-*Cresol–trimethylamine complex*			
0·479932	0·001832	0·001234	2·0323	1·2848	0·000737	240·2
0·445901	0·001609	0·001444	2·0352	1·2843	0·000787	237·8
0·496711	0·001816	0·001992	2·0388	1·2839	0·001018	237·1
	*cyclo*Hexane	—	2·0142	1·2850	—	—

$K = 650 \pm 100$; ${}_Tp_3 = 0{\cdot}6652$ c.c.; * ${}_\infty P_3 = 31{\cdot}3$ c.c.*
Hence, average ${}_TP_4 = 238{\cdot}4$ c.c.; $\mu = 3{\cdot}02 \pm 0{\cdot}02$ D.

			α-*Naphthol–trimethylamine complex*			
0·469264	0·001107	0·000242	2·0201	1·2921	0·000162	261·4
0·470012	0·001216	0·000408	2·0230	1·2929	0·000272	264·6
0·489603	0·001154	0·000352	2·0222	1·2921	0·000231	275·9
	*cyclo*Hexane	—	2·0149	1·2922	—	—

$K = 1000 \pm 200$; ${}_Tp_3 = 0{\cdot}5935$ c.c.; † ${}_\infty P_3 = 45{\cdot}5$ c.c.†
Hence, average ${}_TP_4 = 267{\cdot}3$ c.c.; $\mu = 3{\cdot}14 \pm 0{\cdot}05$ D.

TABLE 2. (*Continued.*)

s	*a*	*b*	*c*	*v*	*x*	$_TP_4$
			β-Naphthol–trimethylamine complex			
0·477239	0·000890	0·000402	2·0221	1·2919	0·000291	364·4
0·490948	0·001029	0·000438	2·0231	1·2917	0·000328	371·6
*cyclo*Hexane		—	2·0150	1·2922	—	—
0·467755	0·001033	0·000448	2·0254	1·2919	0·000310	348·1
*cyclo*Hexane		—	2·0150	1·2922	—	—

$K = 2100 \pm 400$; $_Tp_3 = 0{\cdot}6568$ c.c.;† $_EP_3 = 45{\cdot}5$ c.c.†
Hence, average $_TP_4 = 361{\cdot}4$ c.c.; $\mu = 3{\cdot}80 \pm 0{\cdot}08$ D.

			p-*Chlorophenol–trimethylamine complex*			
0·470831	0·003213	0·003720	2·1334	1·2897	0·002391	436·44
0·472245	0·003213	0·003577	2·1296	1·2904	0·002533	417·53
0·437883	0·003372	0·003949	2·1660	1·2892	0·003359	413·1
*cyclo*Hexane		—	2·0170	1·2950	—	—

$K = 1700 \pm 300$; $_Tp_3 = 1{\cdot}0859$ c.c.;* $_EP_3 = 31{\cdot}6$ c.c.*
Hence, average $_TP_4 = 422{\cdot}3$ c.c.; $\mu = 4{\cdot}30 \pm 0{\cdot}08$ D.

			p-*Fluorophenol–trimethylamine complex*			
0·448273	0·001753	0·000941	2·0445	1·2844	0·000746	369·7
0·454988	0·001154	0·000801	2·0380	1·2844	0·000554	381·4
0·463336	0·001541	0·000838	2·0397	1·2843	0·000643	365·1
*cyclo*Hexane		—	2·0142	1·2851	—	—

K (assumed) $= 1700$; $_Tp_3 = 1{\cdot}0695$ c.c.;‡ $_EP_3 = 38{\cdot}6$ c.c.‡
Hence, average $_TP_4 = 372{\cdot}1$ c.c.; $\mu = 3{\cdot}93 \pm 0{\cdot}04$ D.

			Indole–trimethylamine complex			
0·470194	0·002428	0·002549	2·0469	1·2828	0·0006263	214·1
0·487530	0·001996	0·003123	2·0532	1·2823	0·0006084	261·7
0·470423	0·001751	0·004416	2·0665	1·2807	0·0007029	218·1
*cyclo*Hexane		—	2·0140	1·2848	—	—
0·464169	0·001681	0·002370	2·0455	1·2832	0·0004391	263·3
*cyclo*Hexane		—	2·0142	1·2851	—	—

$K = 85$; $_Tp_3 = 1{\cdot}0452$ c.c.;§ $_EP_3 = 36{\cdot}5$ c.c.§
Hence, average $_TP_4 = 239{\cdot}3$ c.c.; $\mu = 2{\cdot}99 \pm 0{\cdot}18$ D.

			Triphenylmethanol–trimethylamine complex			
0·504443	0·000783	0·000389	2·0185	1·2913	0·0000535	161·1
0·497091	0·001051	0·000494	2·0197	1·2911	0·0000868	162·6
0·474395	0·001029	0·000581	2·0204	1·2908	0·0001027	151·8
*cyclo*Hexane		—	2·0149	1·2921	—	—

$K = 110 \pm 20$; $_Tp_3 = 0{\cdot}4878$ c.c.; $_EP_3 = 83{\cdot}05$.
Hence, average $_TP_4 = 158{\cdot}5$ c.c.; $\mu = 1{\cdot}65 \pm 0{\cdot}06$ D.

* Donle and Gehrckens, *Z. phys. Chem.*, 1932, *B*, **18**, 316.
† Higashi, *Bull. Inst. Phys. Chem. Res. Tokyo*, 1933, **12**, 780.
‡ Leonard and Sutton, *J. Amer. Chem. Soc.*, 1948, **70**, 1564.
§ Cowley and Partington, *J.*, 1936, 47.

DISCUSSION

The results obtained, together with other relevant matter, are shown in Table 3. From the gross moment of the complex, the moments of trimethylamine and of the acidic component, and from a knowledge of the directions of these moments relative to their

TABLE 3.

Acid	μ_{acid}	$\mu_{complex}$	$\Delta\overline{\mu}$	$\Delta\mu$	K	$10^{19}k$
β-Naphthol	1·53	3·80 ± 0·08	—	1·41	2100 ± 400	1·17
p-Chlorophenol	2·22	4·30 ± 0·08	1·26	1·22	1700 ± 300	1·32 *
α-Naphthol	1·41	3·41 ± 0·05	—	0·87	1000 ± 200	1·40
Phenol	1·53	3·24 ± 0·03	1·00	0·84	800 ± 200	1·10
o-Cresol	1·41	3·02$_5$ ± 0·02	—	0·75	650 ± 100	0·63
p-Cresol	1·57	3·13 ± 0·06	0·91	0·70	600 ± 100	0·67
Triphenylmethanol	1·46	1·65 ± 0·06	—	−0·67	110 ± 20	—
Indole	2·05	2·99 ± 0·18	—	(0·08)	85 ± 15	—

* In aqueous ethanol (30% ethanol by volume), Bennett, Brooks, and Glasstone, *J.*, 1935, 1821. Electric dipole moment values are from Wesson, "Tables of Electric Dipole Moments," Massachusetts Institute of Technology Press, 1948.

respective atomic frameworks, it should be possible to calculate the vector changes of dipole moment which occur when the complex is formed. This is, in fact, practicable if the direction of the moment of the acidic component can be taken as fixed relative to the –X–H bond. Otherwise, the problem is not rigorously soluble with the information that we can hope to have available. This condition is satisfied by *p*-substituted phenols, but not by *o*- or *m*-substituted ones, the naphthols, or indole. Accordingly, this calculation has been done for the complexes formed with phenol, *p*-cresol, and *p*-chlorophenol; the results are given in the Table under $\Delta\bar{\mu}$. A less clearly significant measure of the interaction, but one which is easy to calculate, is the scalar difference of moment between that of the complex and the sum of those for the amine and for the acidic component : these values are given under $\Delta\mu$. In addition, the association constant, K, and the acidic dissociation constants in water, k, are included (cf. Table 3 of preceding paper).

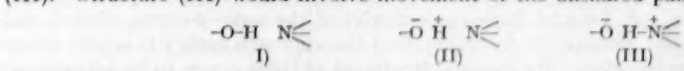
For the calculation of $\Delta\bar{\mu}$ the direction of the resultant moment of the *p*-substituted phenol, relative to the 1 : 4-axis therein, was obtained by vectorial combination of the moments of this substance, of phenol itself, and of the corresponding substituted benzene (*e.g.*, *p*-cresol, phenol, and toluene); and the following values were found :

Phenol, 91°; *p*-cresol, 101°, *p*-chlorophenol, 44° (the values of 101° and 44° mean that the resultant vector is respectively obtuse and acute relative to the O–C bond). The C–O–H angle was assumed to be 120°, the O–H · · · N bond was assumed to be linear, and the moment of trimethylamine was taken to be 0·86 D (Le Fèvre, *Trans. Faraday Soc.*, 1947, **43**, 374).

The errors quoted for $\mu_{complex}$ reflect only the uncertainties of the polarisation measurements (see p. 3902). The effect of uncertainty in K has, however, been considered. A 20% error in K produces the following errors in $\mu_{complex}$: for β-naphthol 0·6%, for α-naphthol 2·5%, for phenol 3%, for *p*-cresol 2·5%; while a 12% error in K for indole gives a 6% error in the moment. The error from this cause in the moments of the more stable complexes is therefore relatively small.

It is immediately apparent from the $\Delta\bar{\mu}$ values that (*a*) there is an appreciable increase of moment when the complex is formed, *i.e.*, the positive pole of the moment thus generated is towards the amine nitrogen atom, (*b*) the increase with *p*-cresol is less than that with phenol, while that with *p*-chlorophenol is greater. Some of this change is probably due to the induction of moments by trimethylamine in the phenol and *vice versa*. Now, such induction as arises in those parts of the molecules outside the O–H bond of the phenol and the N atom of the amine may be considered as extraneous to that which is proper to the formation of the hydrogen bond; but induction within this bond and in this atom is a classical, electrostatic interpretation of the perturbation arising therefrom. Interest is focused especially on the changes which occur between the hydrogen atom and the nitrogen atom, but the change in the O–H bond is coupled with this, so it is to be regarded as part of the whole change due to hydrogen-bond formation. Accordingly, it is necessary only to estimate the extraneous induced moments : this can be done, *e.g.*, by Hampson and Weissberger's method (*J.*, **1936**, 393) which gives a value of the order of 0·2 D.

It is, therefore, reasonably certain that the major part (*ca.* 0·8 D) of the change of moment observed is due to bond formation proper. The non-classical significance of this may be shown as follows. If we adopt the simple view that the actual O–H bond may be described as a resonance hybrid of a covalent and of an ionic structure (I and II respectively), we could say that the only way in which the hydrogen atom can form any but a rigid dipole complex with the amine, involving no deformation of the nitrogen atom, would be through the ionic structure (II) which would make possible an " ammonium " structure (III). Structure (III) would involve movement of the unshared pair of electrons on the



I) (II) (III)

nitrogen atom towards the proton, and a transfer of a formal positive charge from hydrogen to nitrogen, so its formation would generate a moment of $el_{(H\ldots N)}$. If $l_{(H\ldots N)}$ be taken as 1·5 Å, this is 7·2 D; or if 2·0 Å then 9·6 D. The actual change attributed to this cause being only about 0·8 D, we conclude that structure (III) contributes to the extent of not more

than 10%. According to Pauling's estimate that the O–H bond (in water) is 39% ionic (" Nature of the Chemical Bond," Cornell Univ. Press, 1940, Chap. 2), the contributions of the three forms, ignoring any perturbation of the O–H bond by the proximity of the amine, would be: (I) 61%, (II) 29%, and (III) 10%. Since structures (II) and (III) would be the only ones, on this point of view, which contribute to any kind of hydrogen bond, we could then say that this bond is about 75% ionic [(II)/(II + III)] and 25% covalent [(III)/(II + III)]. This is equivalent to saying that there is resonance between a " no-bond " state (I) and a polar bond state (II and III). The perturbing effect of the amine will actually increase somewhat the contribution of structure (II), perhaps to 40%, and part of the moment change will be due to this, so that a better assessment of the hydrogen bond character in this instance seems likely to be 80% ionic and 20% covalent, or even 85% ionic and 15% covalent.

It is interesting to compare these conclusions with estimates made by using Pauling's formalism.* According to this, the electronegativity of the nitrogen atom in structure (III) would be increased to about 3·3 by its positive charge. The difference (1·2) between this and hydrogen would give the bond 30% ionic character only. However, the proximity of the $-O^-$ ion will, in effect, decrease the electronegativity of the hydrogen atom and increase that of the nitrogen atom, so that the actual difference of electronegativity may well be about 2·2, which corresponds to 70% ionic character, and even more. This picture is not necessarily to be accepted as correct; but it provides a useful way of presenting and of discussing the results.

No precise conclusions can be drawn as to the origin of the hydrogen-bond energy; but some interesting qualitative ones emerge. Two rigid dipolar systems have a negative energy of approach; but, *ex definitio*, there could be no dipole moment change, $\Delta\bar{\mu}$, of the complex relative to the correct vector sum of the moments of the two components, so $\Delta\mu$, the scalar difference, could only be zero or negative. This energy may be calculated (cf. Moelwyn-Hughes, *J.*, 1938, 1243; Davies, *Trans. Faraday Soc.*, 1940, **36**, 341) from the bond moments and the interatomic distances, and this has been done by Dr. A. Gilchrist. The most important assumptions are that the O · · · N distance is 3·0 Å (cf. the N–H · · · O bond length; Pauling, *op. cit.*, p. 334), and the O–H bond length is 1·04 Å (increased from 0·97 Å by the perturbation, cf. Davies, *Ann. Reports*, 1946, **43**, 17), making the N · · · H distance 1·96 Å. The other bond lengths are all taken to have the standard values (see *e.g.*, Pauling, *op. cit.*; Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46). Formal charges can then be calculated for each atom: the O–H moment has been taken as 2·3 D by adding to the conventional value (Pauling, *op. cit.*) the whole of the increase of 0·8 D calculated as the actual $\Delta\mu$, in order to make the calculated approach energy as large as possible, μ(C–O) is taken as 0·8 D, μ(C–N) as 0·31 D, and μ(H–C) as 0·30 D. The dielectric constant (ε) of the medium between the charges is taken to be unity which would be strictly correct if the system were electrically non-polarisable. The energy decrease then calculated is *ca.* 3 kcal./mole. It is very sensitive to the value assumed for l(H · · · N): if this were decreased to 1·5 Å (cf., the O · · · O distance, Pauling, *op. cit.*) the energy would be doubled. On the other hand, the effective value of ε must be somewhat greater than unity: if it were equal to the macroscopic value for hydrocarbons it would be *ca.* 2, and the energy would be halved. The correct value of $-\Delta H$ for rigid dipoles is therefore unlikely to exceed 3 kcal./mole. If, now, the dipolar systems be considered polarisable, this energy is found to be increased, but only by *ca.* 0·1 kcal./mole (ε again assumed to be unity), so classical electrostatic calculations can account for only about a half of the observed 5·8 kcal./mole of approach energy.

The qualitative parallel between the $\Delta\bar{\mu}$ values (0·91, 1·00, and 1·26 D respectively) and the $-\Delta H$ values (3·8, 5·8, 7·0 kcal./mole respectively) of the series *p*-cresol, phenol, and *p*-chlorophenol suggests, despite the foregoing, that the approach energy is largely determined by polarisation processes; the classical treatment of these ceases to be adequate at high field strengths (cf. Coulson, Maccoll, and Sutton, *Trans. Faraday Soc.*, 1952, **48**, 106).

The preceding non-classical interpretation of the $\Delta\bar{\mu}$ value in terms of a resonance

* In discussion in 1948, Professor Pauling made suggestions which the senior author believes to be reproduced in essence here.

between ionic and covalent structures cannot be used at all precisely to obtain a revised estimate of the polarisation energy, but if the primitive assumption be made that the contribution of the 10% of covalent character for the N · · · H bond adds 10% of the covalent N–H bond energy (taken as $\frac{1}{2}[H(\text{N–N}) + H(\text{H–H})]$, this increment is 6·2 kcal./mole, which is more than enough to close the gap between the estimated rigid dipole energy and the observed value. It seems likely, therefore, that a considerable part of the energy of these hydrogen bonds is due to the development of covalency between H and N.

The ΔH value mainly determines ΔF and hence K at 25° (see preceding paper). Moreover, there is a parallel between the K values and the acid dissociation constants in water (k). Therefore, since ΔH must be a function of the polarity * of the phenolic O–H bond, whatever the precise mechanism may be, it follows that K must be mainly so determined, and there is an indication that k must be too. The existence of a connection between k and the polarity of the bond from which the proton is released has long been accepted, but the present demonstration is a relatively direct one. The absence of any relation between K and k for benzenethiol shows, however, that the connection is not general.

The $\Delta\mu$ values have the same sequence as the $\Delta\bar{\mu}$ values. Furthermore, for the complexes generally, the $\Delta\mu$ and the K values are monotonically related (see below). In

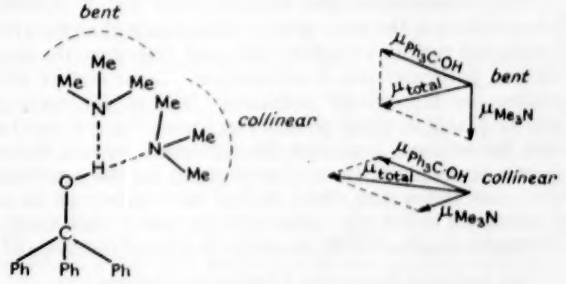


FIG. 1. *The extreme configurations for the triphenylmethanol–trimethylamine complex, and their total electric dipole moments.*

the less stable complex formed with indole there is very little moment change at all, which indicates " rigid dipole " association and hence a low polarity for the N–H bond.

The negative change found for the triphenylmethanol complex requires comment. Although the concentration of the complex, x, is small in the solutions examined, because the solubility of the carbinol in *cyclo*hexane is low and because K is small, the consistency of the calculated total polarisations is about average. Also, although error in K affects $\Delta\mu$, the error to account for a change in μ of 0·7 D would be impossibly large. It would therefore appear that the effect is real. The most probable explanation is that, as may be seen from a model, the repulsion between the methyl groups of the amine and the phenyl groups of the carbinol causes the axis of the amine to incline towards that of the triphenylmethyl group, and so to bend the O–H · · · N system which otherwise would be linear. This would cause the angle between the phenolic moment and the amine moment to increase, and possibly even to become obtuse (see Fig. 1 wherein the extremes are shown) and so would reduce the moment of the complex to less than the scalar sum of these two.

It is surprising to find that $(\Delta\mu)^2$ is a fairly linear function of K (Fig. 2). On a very simple polarisation treatment of hydrogen-bond formation, as being due to the approach energy between a permanent point dipole and a point of polarisability α, it follows that $E = -(\Delta\bar{\mu})^2/2\alpha$, but the observed relation does not follow rigorously from this result. Nevertheless, it appears sufficiently established to be used as follows. In the preceding paper the association constant K for the β-naphthol complex was anomalously large as judged by the value of k for this acid. From Table 3 it is clear that this is due to the bond's being stronger

* The term " polarity" in this context may include not only the permanent moment of the bond but the axial polarisability.

than for the α-naphthol, because $\Delta\mu$ is 1·41 D for the β- and 0·87 D for the α-complex. That the value of the former is the higher cannot be attributed to an error in K for the β-complex relative to that for the α-complex, because if it were in fact the same as the latter, *i.e.*, 1000 instead of the 2100 reported, $\Delta\mu$ would be still higher for the β-complex, *viz.*, 1·9 D; the point would not then fall on the curve in Fig. 2.

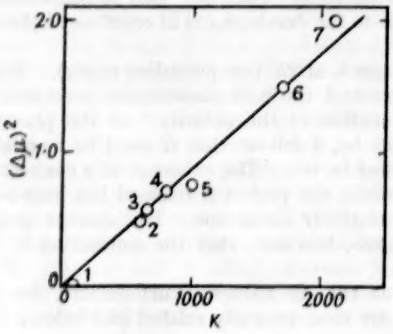


FIG. 2. *The relation between* $(\Delta\mu)^2$ *and* K.
1, Indole; 2, *p*-cresol; 3, *o*-cresol; 4, phenol; 5, α-naphthol; 6, *p*-chlorophenol; 7, β-naphthol.

The monotonic relation between $(\Delta\mu)^2$ and K therefore confirms that the β-complex is anomalous in the sense given; this implies that the greater polarity of the O–H bond in β-naphthol than in α-naphthol does not determine the relative ease of dissociation in water for that particular pair of compounds. Some further indication that the O–H moment is greater in the former substance is that its total electric dipole moment is the greater (Table 3) although this fact by itself is not conclusive. It may also be mentioned that the evidence is against the difference between the naphthols being the result of the greater screening of the hydroxyl group, by the *peri*-hydrogen atom, in the α-compound: were this the reason, there should be evidence of screening in *o*-cresol compared with *p*-cresol, yet in fact the values of K, $\Delta\mu$, and of k are hardly distinguishable. The discussion of possible reasons for this anomaly is beyond the scope of the present paper.

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A New Synthesis of Flavonols of the Quercetagetin Series.

By A. C. JAIN, T. R. SESHADRI, and K. R. SREENIVASAN.

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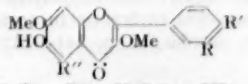
" *ortho*-Oxidation " has been employed for a new synthesis of the flavonols of the quercetagetin series. 6-Hydroxy-3 : 7-dimethoxyflavone yields its 5-aldehyde and thence 5 : 6-dihydroxy-3 : 7-dimethoxyflavone. On methylation it forms the tetramethyl ether of 6-hydroxygalangin. In the same way tangeretin, quercetagetin hexamethyl ether, and melisimplexin have been prepared. Melisimplin has been obtained by partial methylation of the appropriate 5 : 6-dihydroxy-compound.

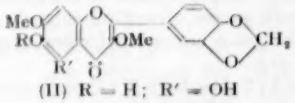
QUERCETAGETIN was synthesised by Baker, Nodzu, and Robinson (*J.*, 1929, 74), from 2 : 6-dihydroxy-ω : 4 : 5-trimethoxyacetophenone, and the same method was later used for the synthesis of tangeretin by Goldsworthy and Robinson (*J.*, 1937, 46). The synthesis was considerably simplified by Row and Seshadri (*Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 24), using the more easily available 2 : 5-dihydroxy-ω : 4 : 6-trimethoxyacetophenone, and they prepared all the members of the series, *i.e.*, 6-hydroxy-derivatives of galangin, kæmpferol, quercetin, and myricetin. Melisimplin and melisimplexin were also synthesised by Briggs and Locker by this procedure (*J.*, 1950, 2379).

Row and Seshadri's method was based on a theory of biogenesis. A purely synthetic

route, using the two-stage "*ortho*-oxidation" of 6-hydroxy-3 : 7-dimethoxyflavones has now been worked out : a 5-aldehyde group is introduced by means of hexamethylenetetramine and then replaced by hydroxyl by treatment with hydrogen peroxide. In the simplest example, 6-hydroxyflavone was earlier converted into 5 : 6-dihydroxyflavone by Seshadri and Viswanadham (*Proc. Indian Acad. Sci.*, 1951, **33**, *A*, 148). The general method is now found to have two advantages over earlier methods : (i) The required intermediates are easily prepared from a cheaper starting material, resorcinol. (ii) The yield of the final product is good and the partial methyl ethers with free 5- and 6-hydroxyl groups are obtained as important intermediates; a compound of this type is oxyayanin-B which was recently isolated by King, King, and Stokes (*J.*, 1954, 4587) from Ayan wood. The compounds listed under the formulæ, and their completely methylated derivatives, have thus been prepared. From the flavone (II; R = H, R′ = OH) partial methylation gives melisimplin (II; R = Me, R′ = OH) and complete methylation gives melisimplexin (II; R = Me, R′ = OMe).



(I) R = R′ = H, R″ = OH
R = H, R′ = OMe, R″ = OH
R = R′ = OMe, R″ = OH



(II) R = H; R′ = OH

Experimental

All the aldehydes and 5 : 6-dihydroxyflavones give the same colour reactions as given for the first examples.

5-Aldehydo-6-hydroxy-3 : 7-dimethoxyflavone (I; R = R′ = H, R″ = CHO).—A solution of 6-hydroxy-3 : 7-dimethoxyflavone (1·9 g.) (Rao, Row, and Seshadri, *Proc. Indian Acad. Sci.*, 1945, **22**, *A*, 30) in glacial acetic acid (75 c.c.) was heated with hexamine (6 g.) on a boiling-water bath for 8 hr. and the resulting reddish solution was further heated with hydrochloric acid (1 : 1; 40 c.c.) for 30 min. After dilution with water and cooling, a pale yellow precipitate separated. It was collected and crystallised from methyl acetate, the *aldehyde* separating as thick yellow plates, m. p. 194—195° (1·5 g.) (Found : C, 66·0; H, 4·0. $C_{18}H_{14}O_6$ requires C, 66·2; H, 4·3%). It gave a reddish-brown colour with ferric chloride and an orange-red colour with concentrated sulphuric acid. Its 2 : 4-dinitrophenylhydrazone separated as orange-yellow needles, m. p. 294° (decomp.), from glacial acetic acid.

5 : 6-Dihydroxy-3 : 7-dimethoxyflavone (I; R = R′ = H, R″ = OH).—To the above aldehyde (1·12 g.), suspended in 6% aqueous sodium hydroxide (12 c.c.), enough pyridine (60 c.c.) was added to yield a clear solution which was cooled to 10°, treated with 6% hydrogen peroxide (5·5 c.c.) in 15 min. with shaking, left at room temperature for 2 hr., then neutralised, and extracted with ether. The residue of *dihydroxyflavone* left on evaporation of the ether solution crystallised from methyl alcohol as yellow rectangular plates, m. p. 171—172° (0·4 g.) (Found : C, 64·9; H, 4·5. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%). It gave a brilliant green colour with ferric chloride and a yellow solution with sulphuric acid. With aqueous (5%) sodium hydroxide, it became red and then blue and eventually dissolved to give a golden-yellow solution which exhibited a pale green fluorescence and yielded a brown precipitate when heated. The acetate crystallised from methyl alcohol as colourless rectangular tablets and rods, m. p. 190—191°. Complete methylation was effected by heating the phenol with excess of methyl sulphate and potassium carbonate in acetone until the product gave a negative ferric reaction; 3 : 5 : 6 : 7-tetramethoxyflavone crystallised as colourless flat needles and rectangular plates, m. p. 110—111° (cf. Row and Seshadri, *loc. cit.*).

5-Aldehydo-6-hydroxy-3 : 7 : 4′-trimethoxyflavone (I; R = H, R′ = OMe, R″ = CHO).—6-Hydroxy-3 : 7 : 4′-trimethoxyflavone (Rao, Row, and Seshadri, *loc. cit.*) (2·1 g.) was condensed with hexamine (7·5 g.) in glacial acetic acid (75 c.c.) as in the earlier case. The *aldehyde* crystallised from methyl acetate as yellow prisms, m. p. 211—212° (1·4 g.) (Found : C, 63·7; H, 4·7. $C_{19}H_{16}O_7$ requires C, 64·0; H, 4·5%). The 2 : 4-dinitrophenylhydrazone crystallised from acetic acid as deep red needles, m. p. 296—297° (decomp.).

5 : 6-Dihydroxy-3 : 7 : 4′-trimethoxyflavone (I; R = H, R′ = OMe, R″ = OH).—The preceding aldehyde (1 g.) was oxidised as described above. The *product* crystallised from alcohol as golden-yellow rhombohedral plates, m. p. 176—177° (0·45 g.) (Found : C, 62·3; H, 5·0.

$C_{16}H_{16}O_7$ requires C, 62·8; H, 4·7%). The diacetate (prepared by acetic anhydride–pyridine) formed colourless needles, m. p. 170—172°, from ethyl acetate. Methylation yielded 3 : 5 : 6 : 7 : 4′-pentamethoxyflavone (tangeretin) as rectangular plates, m. p. 153—154° (cf. Goldsworthy and Robinson, *loc. cit.*).

5-Aldehydo-6-hydroxy-3 : 7 : 3′ : 4′-tetramethoxyflavone (I; R = R′ = OMe, R″ = CHO).—6-Hydroxy-3 : 7 : 3′ : 4′-tetramethoxyflavone (m. p. 223—224°) (Row and Seshadri, *Proc. Indian Acad. Sci.*, 1945, **21**, *A*, 159) (5 g.) and hexamine (15 g.) were heated in glacial acetic acid (130 c.c.) on a boiling water-bath for 7 hr. After acid-treatment the *product* (2·5 g.) crystallised from methyl acetate as golden-yellow rhombohedral prisms, m. p. 202—203° (Found : C, 61·5; H, 4·6. $C_{20}H_{18}O_8$ requires C, 62·1; H, 4·6%). Its 2 : 4-dinitrophenylhydrazone formed orange-red needles (from acetic acid), m. p. 286—287° (decomp.).

5 : 6-Dihydroxy-3 : 7 : 3′ : 4′-tetramethoxyflavone (I; R = R′ = OMe, R″ = OH).—The preceding aldehyde (2·3 g.) was subjected to Dakin oxidation; the *product* crystallised from ethyl acetate as orange-yellow rhombohedral prisms, m. p. 220—221° (1·0 g.) (Found : C, 64·2; H, 4·8. $C_{19}H_{18}O_8$ requires C, 64·4; H, 5·1%). The diacetate crystallised from ethyl acetate as rectangular rods and prismatic needles, m. p. 223—224°. The dihydroxy-flavone, when methylated with excess of methyl sulphate and potassium carbonate in acetone for 60 hr., yielded quercetagetin hexamethyl ether as prismatic needles, m. p. 141—142° (cf. Row and Seshadri, *loc. cit.*).

6-Hydroxy-3 : 7-dimethoxy-3′ : 4′-methylenedioxyflavone (II; R = R′ = H).—A mixture of 2 : 5-dihydroxy-ω : 4-dimethoxyacetophenone (4 g.) (Row and Seshadri, *loc. cit.*), piperonylic anhydride (17 g.) (Rao and Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 148), and potassium piperonylate (6 g.) was heated in a vacuum at 180° for 4 hr. and the product was refluxed with alcoholic 10% potassium hydroxide (200 c.c.) for 0·5 hr. The solvent was removed under reduced pressure and the residual mixture diluted with water and then saturated with carbon dioxide. The solid *flavone* (3·5 g.) was collected and crystallised from alcohol as needles, m. p. 213—214° (Found : C, 63·2; H, 4·1. $C_{18}H_{14}O_7$ requires C, 63·2; H, 4·1%). It was sparingly soluble in aqueous sodium hydroxide and in common organic solvents. With magnesium and hydrochloric acid it gave a brilliant red colour and with sulphuric acid a yellow solution. The monoacetate crystallised from ethyl acetate–light petroleum as colourless rectangular prisms, m. p. 202°.

5-Aldehydo-6-hydroxy-3 : 7-dimethoxy-3′ : 4′-methylenedioxyflavone (II; R = H, R′ = CHO).—The foregoing flavone (2·1 g.) was condensed with hexamine (6·3 g.) in acetic acid; the *aldehyde* (1·2 g.) crystallised from alcohol as pale yellow needles, m. p. 248—249° (Found : C, 61·4; H, 4·2. $C_{19}H_{14}O_8$ requires C, 61·6; H, 3·8%). It readily yielded a 2 : 4-dinitrophenylhydrazone as small red prisms, m. p. 299—300° (decomp.).

5 : 6-Dihydroxy-3 : 7-dimethoxy-3′ : 4′-methylenedioxyflavone (II; R = H, R′ = OH).—The aldehyde (0·9 g.) was subjected to Dakin oxidation; the *dihydroxy-compound* crystallised from methyl acetate as pale yellow needles, m. p. 218—219° (Found : C, 60·7; H, 4·0. $C_{18}H_{14}O_8$ requires C, 60·3; H, 3·9%), sparingly soluble in 5% aqueous sodium hydroxide; the alkaline solution, when heated, afforded an orange salt. The acetate (prepared by acetic anhydride–perchloric acid) crystallised from ethyl acetate–light petroleum as colourless needles, m. p. 226—227°.

Melisimplin (II; R = Me, R′ = OH).—The preceding dihydroxyflavone (100 mg.) was refluxed in acetone (100 c.c.) with methyl sulphate (0·03 c.c.) and potassium carbonate (1 g.) for 8 hr. The solvent was distilled off and the residue was treated with water. The insoluble melisimplin (70 mg.) crystallised from ethyl acetate as yellow needles, m. p. 234—235°. Briggs and Locker (*loc. cit.*) reported m. p. 235—236°. It gave a pink colour with magnesium and hydrochloric acid and a green colour with alcoholic ferric chloride. The acetate (prepared by anhydride–perchloric acid) crystallised from alcohol in colourless needles, m. p. 201—202°.

Melisimplexin (II; R = Me, R′ = OMe).—The 5 : 6-dihydroxyflavone (100 mg.) was methylated with excess of methyl sulphate (0·5 c.c.) by the potassium carbonate–acetone method until the product gave a negative ferric reaction (60 hr.). Melisimplexin crystallised from ethyl acetate as colourless flattened needles, m. p. 184—185°. Briggs and Locker (*loc. cit.*) reported m. p. 185·5°.

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An Improved Technique for Determination of Magnetic Susceptibilities of Solids by the Gouy Method.

By V. C. G. Trew.

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A new technique for measuring magnetic susceptibilities of solids by the Gouy method has been developed. The method has been tested with a crystalline solid and a fine powder and shown to give greater reproducibility than previous methods, especially in the case of the powder. Improved magnetic-susceptibility values have been obtained for potassium chloride and carbon tetrachloride.

Attention has been directed recently to possible sources of error in the determination of the magnetic susceptibility of solids by the Gouy method in which the finely powdered solid is packed into a cylindrical tube. The chief source of error lies in non-uniform packing of the specimen, and the problems of obtaining uniform packing are similar to those found in packing chromatographic columns. It was noted some years ago that this error tends to be particularly high with fine powders and microcrystalline solids, where the usual method of ramming the specimen into the tube tends to produce alternating zones of compressed and lightly packed material. It is generally recognised that reproducibility of results for solid substances is less than that for measurements in the liquid state or in solution. With careful technique and crystals of approximately uniform size, results of any one investigator are usually reproducible within about 1%, but greater divergences may occur, especially between those of different investigators.

French and Harrison (*J.*, 1953, 2538) have moreover drawn attention to the necessity for correcting susceptibility measurements of solids, made by the Gouy method, for the air remaining in the interstices of the packed solid and for the meniscus effect of the calibrating liquid, if such is used. They have also pointed out, with a few figures in support, that uniformity rather than tightness of packing is the limiting factor governing reproducibility. They did not, however, investigate the problem of attaining uniformity of packing, and do not record the number of individual measurements made or the mean error obtained.

The following modification effects a considerable improvement in the uniformity of packing: the susceptibility tube is filled with the solid under investigation by gradual sedimentation under a column of the reference liquid used in calibrating the magnetic balance. By tapping and rotating the tube during sedimentation, and centrifuging slowly at intervals, a high degree of reproducibility was obtained even with finely powdered solids. A number of measurements have been made on the same solid to check the method in detail. Pure potassium chloride was selected as it has been used as a standard for calibration. Some measurements have also been made on a fine powder, thallic oxide being chosen, as some earlier unsatisfactory results, obtained by the ramming technique, were available for comparison.

Experimental

Measurements of the specific susceptibility have been made with two calibrating liquids, various field strengths, and susceptibility tubes of different cross-sectional area. After completion of each set of measurements the liquid was evaporated and a final measurement made with air in the interstices of the solid. Benzene and carbon tetrachloride, in which the inorganic salts under investigation are insoluble, were used as the standard liquids. Benzene has a high susceptibility and has been used for some time as a calibrating standard, while carbon tetrachloride affords a useful alternative for testing the method owing to its low susceptibility and high density. The method of measurement of the magnetic susceptibility and the magnetic balance used have been described previously (Trew and Watkins, *Trans. Faraday Soc.*, 1933, **29**, 1310; French and Trew, *Trans. Faraday Soc.*, 1945, **41**, 439). The volumes of the susceptibility tubes and densities (d_4^{20}) of the liquids and of the solids were determined. Measurements were made of the diamagnetic thrust on the tube alone and filled to the mark

with the standard liquid, before each set of measurements, and these calibrations were repeated after the final measurement with air in the interstices of the material. To pack the tube it was filled about two-thirds of the way to the mark with the standard liquid; the finely powdered solid, after being sieved through a stretched cotton gauze of approx. 40-mesh, was dropped into the tube from a weighing bottle. The tube was lightly tapped and rotated during the addition of solid to ensure even sedimentation. The most reproducible packing was obtained when slow centrifugation was used after about each 0·5-cm. length had been filled. Centrifugation was continued for a minute at 2000 r.p.m., giving a force of 200 ***g*** at the top and 500 ***g*** at the base of the tube. The adjustment of the solid to the upper mark of the standard apparatus was somewhat critical and was best achieved by levelling off at the mark, under the liquid, with a glass rod of dimensions just smaller than those of the tube, while viewing the interface with a strongly magnifying lens. The level of the liquid meniscus was then adjusted with the tube suspended in a thermostat at 20°. Magnetic measurements were made at room temperature,

TABLE 1.

W_{KCl}	W_m	F_m	F_s	χ_m ($\times -10^6$)	χ_{KCl} ($\times -10^6$) (*A*)	χ_{KCl} ($\times -10^6$) (*B*)	F_s	χ_{KCl} ($\times -10^6$) (*C*)
(*a*) Tube 1; packed under benzene. W_s = 2·7289 g. V_1 = 3·104 ml. l_s = 8·014 cm.								
2·7327	4·2403	16·54	12·95	0·5832	0·5175	0·5144	9·56	0·5207 [1]
3·1685	4·4003	15·89	12·18	0·5702	0·5188	0·5087	10·26	0·5092
3·2599	4·5511	15·90	11·86	0·5715	0·5196	0·5206	10·41	0·5240 [2]
3·2354	4·5332	15·87	11·88	0·5725	0·5186	0·5186	10·29	0·5226
2·9617	4·3797	15·41	11·86	0·5750	0·5138	0·5136		
3·3521	4·5974	15·83	11·86	0·5634	0·5118	0·5113	10·50	0·5084
3·3967	4·6223	15·91	11·86	0·5632	0·5131	0·5125		
(*b*) Tube 2; packed under benzene. W_s = 3·2674 g. V_2 = 3·7242 ml. l_s = 9·01 cm.								
3·4560	5·1755	17·04	13·18	0·5794	0·5182	0·5142	10·26	0·5166 [3]
3·4560	5·1755	16·76	12·97	0·5790	0·5177	0·5137	10·08	0·5154 [4]
3·4560	5·1755	16·49	12·75	0·5796	0·5186	0·5145	9·89	0·5144 [5]
(*c*) Tube 1; packed under carbon tetrachloride. W_s = 4·9505 g.								
3·2344	5·6350	16·51	13·24	0·4795	0·5132 *	0·5194	10·10	0·5179
			11·86	0·4798	0·5137			
3·2344	5·6237	16·50	13·24	0·4803	0·5144	0·5194		
			11·86	0·4804	0·5147			
3·3251	5·6048	16·52	13·24	0·4825	0·5157	0·5149	—	—
			11·86	0·4827	0·5158			
(*d*) Tube 2; packed under carbon tetrachloride. W_s = 5·9362 g.								
4·0159	6·7657	18·26	14·55	0·4827	0·5164 *	0·5186	11·41	0·5139
			13·04	0·4813	0·5136			
4·0159	6·7565	18·26	14·55	0·4832	0·5173	0·5186		
			13·04	0·4819	0·5146			
(*e*) Tube 3; packed under benzene. W_s = 6·6411 g. V_3 = 7·5549 ml.								
8·5678	11·4061	8·94	6·56	0·5640	0·5181	0·5176	—	—
8·6399	11·4655	8·98	6·56	0·5637	0·5183	0·5192	—	—

Mean values χ_{KCl} (*A*) = $-0·5164 \pm 0·0021 \times 10^{-6}$
χ_{KCl} (*B*) = $-0·5159 \pm 0·0029 \times 10^{-6}$
χ_{KCl} (*C*) = $-0·5163 \pm 0·0040 \times 10^{-6}$

* Calc. relative to carbon tetrachloride as standard (upper row), and benzene as standard (lower row).

[1, 2, 3, 4, 5] Length of residual column slightly contracted, to 7·91, 8·00, 8·84, 8·84, and 8·84 cm. respectively.

which rarely varied within the magnet enclosure by more than a degree from 20°. In determinations of the thrust on the mixture the mean of at least six readings was taken for each packing. In some experiments the mixture was then centrifuged again, and again filled to the mark and the thrust re-measured. Some measurements were made at different field strengths, as described in a previous paper (Trew, *Trans. Faraday Soc.*, 1953, **49**, 604), and two sets included were carried out by Dr. S. A. Husain using a different magnet with smaller field and larger susceptibility tubes. The diamagnetic susceptibility of benzene as a standard is well established, but it was found necessary to remeasure that of carbon tetrachloride. Four different field strengths and both susceptibility tubes were used to obtain a mean value of

$-10^6\chi = 0{\cdot}4341 \pm 0{\cdot}0006$ e.m.u. per g., in agreement with an earlier value of $0{\cdot}4340 \pm 0{\cdot}0011$ (French and Trew, *loc. cit.*).

The specific mass susceptibility χ_m of the mixture of solid and liquid was calculated from the relation :

$$\left(\chi_m - \frac{kV}{W_m}\right) \Big/ \left(\chi_s - \frac{k}{d_s}\right) = F_m W_s / F_s W_m$$

an expression used in earlier work with liquids (Trew, *loc. cit.*) but with the ratio of the densities replaced by that of the weights in volume V. χ_s is the specific mass susceptibility of the standard liquid, k the volume susceptibility of air ($0{\cdot}0294 \times 10^{-6}$), and d_s the density of the standard liquid. F_m and F_s are the thrusts in mg. on the column of mixture filling the volume V, and W_m and W_s are the corresponding weights in grams corrected in each case for the meniscus correction of the liquid. This correction was calculated from Bashford and Adams's tables in The International Critical Tables (Vol. I, p. 73).

The specific mass susceptibility χ of the salt then follows by application of the mixture law, *i.e.*, $\chi_m = [p\chi + (1 - p)\chi_s]$, where p is the weight fraction of solid in the mixture. Values of the susceptibility χ_{KCl} (A), calculated in this manner, are recorded in column 6 of Table 1. To test the extent of possible errors introduced by incorrect adjustment of liquid to the mark when the tube is packed with solid, the results χ_{KCl} (B) in column 7 were evaluated. The volume of liquid in the interstices of solid and hence total weight of mixture were here calculated from the known weight and density of solid used and the volume of the tube. The last two columns show the thrust, F_s, obtained on the solid after evaporation of the standard liquid, and the resulting susceptibility χ_{KCl} (C) calculated by means of French and Harrison's formula (*loc. cit.*) with corrections for the meniscus effect and the residual air in the interstices of solid.

A similar set of experiments was carried out with finely powdered thallic oxide, prepared by oxidation of a nearly saturated solution of pure thallous nitrate in 25% aqueous sodium hydroxide by means of 5% hydrogen peroxide at 80°. The resultant precipitated oxide was washed repeatedly by decantation and dried and the thallium estimated as chromate (Found, 89·8. Calc. : 89·5%). The susceptibility results for six determinations with the new technique are recorded in Table 2, where are given also the summarised results of some unsatisfactory earlier measurements (ramming method in air).

TABLE 2.

$W_{Tl_2O_3}$	W_m	F_m	χ_m ($\times -10^6$)	$\chi_{Tl_2O_3}$ ($\times -10^6$)	$W_{Tl_2O_3}$	W_m	F_m	χ_m ($\times -10^6$)	$\chi_{Tl_2O_3}$ ($\times -10^6$)
$W_s = 3{\cdot}2369$ g. $F_s = 12{\cdot}70$ mg. $V_s = 3{\cdot}6865$ cm.									
7·5716	10·064	16·67	0·2997	0·1672	8·0767	10·556	17·07	0·2930	0·1673
7·6284	10·112	16·42	0·2938	0·1608	8·1624	10·543	17·04	0·2929	0·1718
7·7934	10·273	16·67	0·2936	0·1634	8·2658	10·728	17·05	0·2879	0·1645

Mean $\chi_{Tl_2O_3} = -0{\cdot}1658 \pm 0{\cdot}0029 \times 10^{-6}$.

Previous values packed in air by ramming; mean of eleven readings, $-0{\cdot}176 \pm 0{\cdot}026 \times 10^{-6}$, with individual readings ranging from 0·137 to 0·206 $\times 10^{-6}$.

DISCUSSION

For potassium chloride the figures in Table 1 show a much greater reproducibility than is generally found by other methods of packing. The agreement of the mean from columns 6 and 7 shows that with care the error in filling the liquid to the mark is negligible. In addition the mean value from the figures in column 9 affords a striking confirmation of the method. Here, however, the variation between individual results is rather greater as no especial precautions were taken to prevent displacement of the solid during evaporation of the standard liquid, or to see that air entirely replaced all the vapour of the liquid in the interstices. It was noted that uniformity of packing was still the most critical factor in obtaining reproducibility of results. Two sets of figures, one for the solid packed under benzene and one under carbon tetrachloride, in which sedimentation of the potassium chloride was allowed to take place without centrifugation, gave low results and were discarded.

The figures for thallic oxide show that the new technique gives much greater reproducibility on fine powders. The earlier value of $\chi = -0{\cdot}176 \pm 0{\cdot}026 \times 10^{-6}$ is

replaced by the figure of $-0{\cdot}166 \pm 0{\cdot}003 \times 10^{-6}$, a ten-fold improvement in the mean error. The mean specific mass susceptibility of potassium chloride, $-10^6\chi = 0{\cdot}5164 \pm 0{\cdot}0021$, gives a molar susceptibility of $-10^6\chi_M = 38{\cdot}50$. Both this figure and that for carbon tetrachloride supply useful additional standards for diamagnetic measurements. The new method of packing the susceptibility tube should be equally applicable to measurements on paramagnetic solids.

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The Condensation of Phenols with Nitrobenzaldehydes.

By J. E. DRIVER and (MISS) S. F. MOK.

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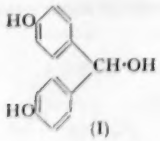
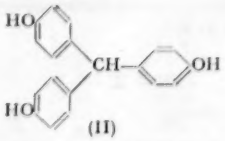
Triphenylmethane derivatives have been isolated (some in high yield) from the products of condensation of phenols with *o*-, *m*-, and *p*-nitrobenzaldehydes. Many of them form molecular compounds with hydrocarbon solvents.

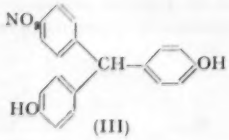
IT has been shown (Driver and Sousa, *J.*, 1954, 985) that if phenols are condensed with hydroxybenzaldehydes at a sufficiently low temperature and in a suitable medium trihydroxytriarylmethanes can be isolated, though usually only in small yield, from the resinous products. The first reaction (as established in a typical case) leads to the formation of a dihydroxydiarylmethanol (as I), which gives the triarylmethane compound (as II) by the preferred *para*-condensation. Resinification may be the result of formation of large molecules by repeated electrophilic attack at positions *ortho* to hydroxyl groups in these and later products.



(I)



(II)



(III)

The use of a deactivated aromatic aldehyde would be expected to make the resulting di- or tri-arylmethane derivatives more easily isolable, since one nucleus in the intermediate methanol, and in the triarylmethane product, would then not be susceptible to further attack by the aldehyde; and further the lower rate of *ortho*-condensation by the less easily protonated aldehyde might be more significant than any reduction in rate of the faster *para*-condensations. The nitrobenzaldehydes were therefore selected for study.

de Varda and Zenoni (*Gazzetta*, 1891, **21**, 174) condensed phenol with *m*-nitrobenzaldehyde and obtained an amorphous product, m. p. 59—60°, which they recorded as 4 : 4′-dihydroxy-3″-nitrotriphenylmethane; from the present work it was clearly a resinous mixture. Chlorine-containing substances were obtained by Guyot and Haller (*Bull. Soc. chim. France*, 1904, **31**, 530) and Zincke and Siebert (*Ber.*, 1906, **39**, 1930) by condensation of phenol with *o*-nitrobenzaldehyde in presence of hydrochloric–acetic acid. Danckwortt (*Ber.*, 1909, **42**, 4163) obtained from phenol and *p*-nitrobenzaldehyde a red resin having a nitrogen content corresponding to a 2 : 1-molecular condensation. King and Lowy (*J. Amer. Chem. Soc.*, 1924, **46**, 760) obtained from the same reactants a yellow, amorphous product from which they prepared a crystalline tetrabromo-derivative; from *p*-nitrobenzaldehyde and other phenols they also obtained only amorphous products. All these experiments were done under what appear to be unfavourable conditions.

It is now shown that crystalline dihydroxynitrotriarylmethanes can be readily prepared by condensing various simple phenols with *o*-, *m*-, and *p*-nitrobenzaldehydes by means of sulphuric acid in cold, acetic acid solution. By reduction they yield the corresponding aminodihydroxy-compounds. The *para*-orientation of a typical compound (III; from

phenol and *p*-nitrobenzaldehyde) has been proved by its reduction to the amine and conversion of this into leucaurin (II).

To demonstrate that resin formation in these reactions results from successive condensations at activated positions, **2 : 6-xylen-1-ol** was condensed with ***m*-nitrobenzaldehyde**. The product, **4 : 4′-dihydroxy-3 : 3′ : 5 : 5′-tetramethyl-3″-nitrotriphenylmethane**, which has no positions open to electrophilic attack, was formed in very high yield and unaccompanied by any significant amount of resin.

Many of the dihydroxynitrotriarylmethanes and the corresponding amines form molecular compounds with aromatic hydrocarbons, usually in stoicheiometric proportions (see Table). Most of these solvated compounds lose solvent freely only above their m. p.s at ordinary rates of heating.

Molecular compounds of substituted triphenylmethanes with aromatic hydrocarbons.

4 : 4′-Dihydroxytriphenylmethane (*A*)	Solvent (*B*)	*A* : *B* (mols.)	Solvent-free compd. from :
3″-Nitro-	Benzene	1 : 2	*p*-Xylene
	Toluene	1 : 1	
2 : 2′-Dimethyl-3″-nitro-	Benzene	1 : 2	—
3 : 3′-Dimethyl-3″-nitro-	Benzene	1 : 1	—
4″-Nitro-	Benzene	1 : 2	—
	Toluene	1 : 1	
2 : 2′-Dimethyl-4″-nitro-	Benzene	1 : 2	—
2″-Nitro-	Benzene	1 : 1	Toluene
3 : 3′-Dimethyl-2″-nitro-	Benzene	2 : 1	—
	Toluene	2 : 1	
3 : 5 : 3′ : 5′-Tetramethyl-3″-nitro-	Benzene	3 : 2	—
	Toluene	3 : 2	
	p-Xylene	3 : 2	
3″-Amino-	Benzene	1 : 1	—
	Toluene	1 : 1	

Experimental

Sulphuric acid and acetic acid used were 99%.
Microanalyses are by Dr. Zimmermann, Melbourne.

Condensation of Phenol and m-*Nitrobenzaldehyde.*—A solution of *m*-nitrobenzaldehyde (7·6 g.) and phenol (9·4 g.) in acetic acid (35 ml.) was cooled to 3—4°, and sulphuric acid (3 ml.) in acetic acid (15 ml.) was added dropwise with stirring. The mixture, which turned orange, was kept at 0—5° for 48 hr., and was then stirred into crushed ice. The resin which separated was washed until free from acid, and freed from adhering water. The solution in hot benzene deposited some red resin on cooling, followed by yellow crystals of the *benzene* compound (10·7 g., 45%) which after recrystallization melted at 72° solidified with slowly continued rise in temperature, and melted again at 156—157° (Found : C, 78·4; H, 5·8; N, 3·1; loss at 100°/25 mm., 32·3. $C_{19}H_{15}O_4N,2C_6H_6$ requires C, 78·1; H, 5·7; N, 2·9; C_6H_6, 32·7%). Unsolvated **4 : 4′-*dihydroxy*-3″-*nitrotriphenylmethane*** separated from aqueous alcohol, ether–light petroleum, *p*-xylene, or chlorobenzene in crystals, m. p. 158·5° (Found : C, 71·3; H, 4·8 N, 4·3%; *M*, 321. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·4%; *M*, 321). The *toluene* compound formed crystals, m. p. 150—157·5° with loss of solvent (Found : loss at 100°/3 mm., 22·0. $C_{19}H_{15}O_4N,C_7H_8$ requires C_7H_8, 22·3%). The *diacetyl* derivative separated from ethyl alcohol in needles, m. p. 98·5° (Found : C, 68·4; H, 4·9; N, 3·7; Ac, 20·9. $C_{23}H_{19}O_6N$ requires C, 68·2; H, 4·7; N, 3·5; Ac, 21·2%). The *dibenzoyl* derivative crystallized from light petroleum or carbon tetrachloride and had m. p. 145—146° (Found : C, 75·0; H, 4·5; N, 2·2. $C_{33}H_{23}O_6N$ requires C, 74·9; H, 4·35; N, 2·6%).

3-*Amino*-4′ : 4″-*dihydroxytriphenylmethane*. (*a*) The nitro-compound (20 g.) in alcohol (100 ml.) was reduced by hydrogen in presence of Adams's catalyst. Absorption of hydrogen (3200 c.c.) was complete in 30 min. The solution was filtered through kieselguhr and the alcohol removed. Extraction of the remaining glue with benzene yielded prisms (2·2 g.) of the amine (as below).

(*b*) Reduction in acid media gave red resins. The nitro-compound (15 g.) in ethyl alcohol (50 ml.) was treated with 12% ammonia solution (10 ml.), and the solution was added to a boiling solution of ferrous sulphate (61·5 g., 7 mols.) in water (150 ml.). After addition of excess of ammonia the mixture was boiled with stirring for 10—15 min., and filtered. The

filtrate and the black residue were extracted with ether. Removal of solvent left a brown residue which was crystallized from benzene to yield the *benzene* compound (6·8 g.) which melted at about 110° with evolution of solvent, solidified thereafter, and melted again at 168° (Found: C, 81·3; H, 6·2; N, 3·9; loss at 116°/25 mm., 21·3. $C_{19}H_{17}O_2N,C_6H_6$ requires C, 81·3; H, 6·2; N, 3·8; C_6H_6, 21·1%. Found for the desolvated compound: C, 78·4; H, 5·9; N, 3·9%; *M*, 488. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·8; N, 4·8%; *M*, 291).

Unsolvated *3-amino-4′ : 4″-dihydroxytriphenylmethane* crystallized from aqueous alcohol and had m. p. 168°. It was not easily soluble in dilute acid, but dissolved freely in aqueous sodium hydroxide. A suspension of the amine in hydrochloric acid was diazotized and coupled with β-naphthol in sodium carbonate–hydrogen carbonate buffer to give a bright-red *dye* which separated as an amorphous solid from glacial acetic acid (Found: N, 6·4. $C_{29}H_{22}O_3N_2$ requires N, 6·3%). The *toluene* compound sintered at 80—90°, solidified again, and melted at 166—168° (Found: C, 81·6; H, 6·6; N, 3·5; loss at 116°/25 mm., 23·4. $C_{19}H_{17}O_2N,C_7H_8$ requires C, 81·5; H, 6·5; N, 3·65; C_7H_8, 24·0%). Attempts to deaminate the amine, or to methylate it with a view to subsequent oxidation, failed.

Condensation of m-*Cresol and* m-*Nitrobenzaldehyde.*—A yield of only 17% by a procedure similar to that used for phenol (time, 7 hr.) was increased to 44% as follows. A solution of *m*-nitrobenzaldehyde (20 g.) and *m*-cresol (30 g.) in acetic acid (50 ml.) was cooled to 0°, and sulphuric acid (2·5 ml.) in acetic acid (15 ml.) was added dropwise with stirring to the crystalline mass. The mixture was kept at 0—5° for 8 hr. and stirred into ice-water, and the product was washed free from acid. The hard resin by crystallization from benzene yielded the *benzene* compound (29 g., 44%) which melted at 85—90° with loss of solvent, then solidified, and melted again at 169—171° (Found: C, 78·2; H, 6·15; N, 2·9; loss at 154°/25 mm., 30·1. $C_{21}H_{19}O_4N,2C_6H_6$ requires C, 78·4; H, 6·2; N, 2·8; C_6H_6, 30·9%). From aqueous alcohol what appeared to be a *hemihydrate* crystallized which melted at 140°, resolidified, and melted again (Found, in the substance dried at 100°/25 mm.: C, 70·8; H, 5·7; N, 4·0; loss at 154°/25 mm., 2·9. $C_{21}H_{19}O_4N,\frac{1}{2}H_2O$ requires C, 70·4; H, 5·6; N, 3·9; H_2O, 2·5%). Unsolvated *4 : 4′-dihydroxy-2 : 2′-dimethyl-3″-nitrotriphenylmethane* had m. p. 171—172° (Found: C, 72·4; H, 5·6; N, 3·6%; *M*, 330. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%; *M*, 349). The *diacetyl* derivative, crystallized from ethyl alcohol, had m. p. 156° (Found: C, 69·7; H, 5·4; N, 3·4; Ac, 19·6. $C_{25}H_{23}O_6N$ requires C, 69·3; H, 5·35; N, 3·2; Ac, 19·9%). The *dibenzoyl* derivative, crystallized from light petroleum, had m. p. 173·5—175° (Found: C, 75·7; H, 5·1; N, 2·8. $C_{35}H_{27}O_6N$ requires C, 75·4; H, 4·9; N, 2·5%).

3-Amino-4′ : 4″-dihydroxy-2′ : 2″-dimethyltriphenylmethane. The solvated nitro-compound (10 g.) in ethyl alcohol (35 ml.) and 12% ammonia solution (6 ml.) was added with stirring to ferrous sulphate crystals (40 g.) in boiling water (100 ml.). Ammonia was added portionwise until the liquid was alkaline, and the mixture was boiled and stirred for 15 min. and filtered. Extraction of the residue and filtrate with ether yielded a viscous liquid which by crystallization from benzene yielded a buff, crystalline powder with a benzene content (7·8—9·8%) which varied with different samples. Crystallization from aqueous alcohol yielded unsolvated *3-amino-4′ : 4″-dihydroxy-2′ : 2″-dimethyltriphenylmethane*, m. p. 245—247° (Found: C, 78·2; H, 6·8; N, 4·3%; *M*, 337. $C_{21}H_{21}O_2N$ requires C, 78·9; H, 6·6; N, 4·4%; *M*, 319).

Condensation of o-*Cresol and* m-*Nitrobenzaldehyde.*—Many condensations under varied conditions yielded orange-red resins from which no crystalline product could be obtained by various methods of separation which included molecular distillation and chromatography. After having been kept for 4 months the resins had partly crystallized, and thereafter the crystalline compound was readily prepared. A solution of *o*-cresol (pure, for cineole determination; 10·8 g.) and *m*-nitrobenzaldehyde (7·55 g.) in acetic acid (40 ml.) was cooled to 4°. To the resulting soft, crystalline mass sulphuric acid (2 ml.) in acetic acid (10 ml.) was added with stirring. After being kept below 0° for 24 hr. the mixture was stirred into ice-water. From the solid product the *benzene* compound (12 g.; 70%) was obtained in yellow crystals, m. p. 63—68° (Found: C, 75·8; H, 5·7; N, 2·5; loss at 132°/2—5 mm., 17·4. $C_{21}H_{19}O_4N,C_6H_6$ requires C, 75·7; H, 5·8; N, 3·3; C_6H_6, 18·3%). Desolvated *4 : 4′-dihydroxy-3 : 3′-dimethyl-3″-nitrotriphenylmethane* sintered at 63° but the m. p. was indefinite; it did not crystallize from solvents other than benzene (Found: C, 71·4; H, 5·65; N, 3·2. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%). The *diacetyl* derivative crystallized from ethyl alcohol in needles, m. p. 163° (Found: C, 69·5; H, 5·55; N, 3·1; Ac, 20·8. $C_{25}H_{23}O_6N$ requires C, 69·3; H, 5·35; N, 3·2; Ac, 19·9%).

Condensation of p-*Cresol and* m-*Nitrobenzaldehyde.*—A solution of *p*-cresol (5·4 g.) and *m*-nitrobenzaldehyde (3·78 g.) in acetic acid (20 ml.) was cooled to 3—4°, and sulphuric acid

(2 ml.) in acetic acid (5 ml.) was dropped in with stirring. After 44 hr. at *ca.* 0° the product was isolated as before. **2 : 2′-*Dihydroxy*-5 : 5′-*dimethyl*-3″-*nitrotriphenylmethane*** was very soluble in most common organic solvents but crystallized from light petroleum (b. p. 80—100°), or a mixture of this with benzene, in clusters of yellow needles, m. p. 144° (Found : C, 72·4; H, 5·55; N, 3·9%; *M*, 336. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%; *M*, 349). The *diacetyl* derivative, crystallized from ethyl or methyl alcohol, had m. p. 131° (Found : C, 69·6; H, 5·2; N, 3·3; Ac, 18·0. $C_{25}H_{23}O_6N$ requires C, 69·3; H, 5·35; N, 3·2; Ac, 19·9%).

Condensation of Phenol and p-*Nitrobenzaldehyde.*—Phenol (9·4 g.) in acetic acid (50 ml.) was added to *p*-nitrobenzaldehyde (7·55 g.) in acetic acid (200 ml.), and the mixture was cooled slowly to 7° with stirring, the hard deposit being continuously broken up. Sulphuric acid (10 ml.) in acetic acid (30 ml.) was added slowly, drop by drop, with cooling, and the mixture kept at between −2° and 0° for 18 hr. The product separated from benzene partly as resin and partly as large, pale yellow prisms of the *benzene* compound (8·5 g., 36%), m. p. 49—57° (Found : loss at 100°/2—5 mm., 32·6. $C_{19}H_{15}O_4N,2C_6H_6$ requires C_6H_6, 32·7%). The *toluene* compound melted at 45—50° (Found : loss at 100°/3 mm., 19·4. $C_{19}H_{15}O_4N,C_7H_8$ requires C_7H_8, 22·3%). Unsolvated **4 : 4′-*dihydroxy*-4″-*nitrotriphenylmethane***, made by removal of benzene from the solvated compound, melted at 86—87° with previous sintering, but did not crystallize from solvents (Found : C, 70·0; H, 4·9; N, 4·1%; *M*, 278. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·4%; *M*, 321). The tetrabromo-derivative, made by brominating the compound in acetic acid, separated from acetic acid in yellow crystals, m. p. 211° [King and Lowy (*loc. cit.*) give m. p. 215° for the tetrabromo-derivative prepared from their amorphous product] (Found : C, 36·4; H, 1·9; N, 2·3; Br, 50·7. Calc. for $C_{19}H_{11}O_4NBr_4$: C, 35·8; H, 1·7; N, 2·2; Br, 50·2%).

4-*Amino*-4′ : 4″-*dihydroxytriphenylmethane*. The nitro-compound (3 g.) was reduced by ferrous sulphate and ammonia as described in the first example. The *amine* crystallized from aqueous alcohol or benzene in unsolvated needles, m. p. 219—221°, with a pink tinge (Found : C, 77·8; H, 5·75; N, 4·8%; *M*, 291. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·8; N, 4·8%; *M*, 291).

Leucaurin. Sodium nitrite (0·15 g.) was added to ice-cold sulphuric acid (1·2 ml.); the mixture was warmed slightly to give a solution, and cooled to 0°. The amine (0·3 g.) in acetic acid (4 ml.) was added dropwise very slowly, the temperature being kept below 10°. The solution was stirred into 40 ml. of boiling water, and boiling was continued until gas ceased to be evolved. The mixture was cooled and extracted with ether. The solid left by evaporation of the ether was crystallized from aqueous alcohol (charcoal) to give long needles of leucaurin, m. p. and mixed m. p. with an authentic sample, 233—235°.

Condensation of m-*Cresol and* p-*Nitrobenzaldehyde.*—*m*-Cresol (2·16 g.) and *p*-nitrobenzaldehyde (1·51 g.) were condensed in acetic acid solution, and the product isolated, as in the first example. The *benzene* compound formed pale yellow crystals which melted at 88—94° with evolution of benzene; the melt resolidified at 100—110° (Found : C, 77·8; H, 6·05; N, 2·9; loss at 132°/3—6 mm., 30·1. $C_{21}H_{19}O_4N,2C_6H_6$ requires C, 78·4; H, 6·2; N, 2·8; C_6H_6, 30·9%). Unsolvated **4 : 4′-*dihydroxy*-2 : 2′-*dimethyl*-4″-*nitrotriphenylmethane*** separated from aqueous alcohol in pale yellow needles, m. p. 203·5—204·5° (Found : C, 72·1; H, 5·6; N, 3·7%; *M*, 380. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%; *M*, 349).

Condensation of p- *and* o-*Cresols and* p-*Nitrobenzaldehyde.*—The yellow product from *p*-cresol was obtained in doubtfully crystalline form, m. p. *ca.* 210—220°, after several separations from *cyclo*hexane. It was not analyzed.

No crystalline product was obtained from *o*-cresol and *p*-nitrobenzaldehyde.

Condensation of Phenol and o-*Nitrobenzaldehyde.*—Phenol (1·88 g.) and *o*-nitrobenzaldehyde (1·51 g.) were condensed and the product isolated as in the first example. The *benzene* compound (yield, 2·0 g., 50%) formed crystals, m. p. 162—163° (Found : loss at 183°/3—4 mm., 19·2. $C_{19}H_{15}O_4N,C_6H_6$ requires C_6H_6, 19·55%). **4 : 4′-*Dihydroxy*-2″-*nitrotriphenylmethane*** separated in unsolvated, pale yellow prisms, m. p. 163°, from alcohol, toluene, or chlorobenzene (Found : C, 71·3; H, 4·8; N, 4·1%; *M*, 651. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·4%; *M*, 321).

Condensation of m-*Cresol and* o-*Nitrobenzaldehyde.*—*m*-Cresol (5·4 g.) and *o*-nitrobenzaldehyde (3·8 g.) were condensed as in the first example (time, 42 hr.). The product, **4 : 4′-*dihydroxy*-2 : 2′-*dimethyl*-2″-*nitrotriphenylmethane***, separated from benzene in unsolvated yellow needles, m. p. 236—238°; it was also crystallized from light petroleum, *cyclo*hexane, and ethyl alcohol, but from all solvents many recrystallizations (charcoal) were necessary to free it from resin (Found : C, 71·6; H, 5·7; N, 4·3. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%).

Condensation of p-*Cresol and* o-*Nitrobenzaldehyde.*—*p*-Cresol (5·4 g.) and *o*-nitrobenzaldehyde (3·8 g.) were condensed as in the first example (time, 24 hr.). The product crystallized readily

from benzene, toluene, aqueous alcohol, or light petroleum (yield, 5·1 g., 66%); the crystals from all these retained small proportions of solvent which lowered the m. p. by several degrees. 2 : 2′-*Dihydroxy*-5 : 5′-*dimethyl*-2″-*nitrotriphenylmethane*, dried at 160°/3 mm., had m. p. 176—177° (Found : C, 72·5; H, 5·75; N, 4·0%; *M*, 337. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%; *M*, 349).

Condensation of o-Cresol and o-Nitrobenzaldehyde.—*o*-Cresol (10·8 g.) and *o*-nitrobenzaldehyde (7·55 g.) were condensed as in the first example (time, 24 hr.). The orange-red product yielded stout, yellow prisms of the *benzene* compound, m. p. 100—110° (indefinite) (yield, 7·5 g., 50%), and some dark red resin (Found : loss at 116°/3—5 mm., 10·5. $2C_{21}H_{19}O_4N,C_6H_6$ requires C_6H_6, 10·1%). The *toluene* compound melted at 95—110° (Found : loss at 116°/3—5 mm., 12·05. $2C_{21}H_{19}O_4N,C_7H_8$ requires C_7H_8, 11·6%). The *chlorobenzene* compound melted at 85—100° (Found : loss at 116°/3—5 mm., 21·7. $C_{21}H_{19}O_4N,C_6H_5Cl$ requires C_6H_5Cl, 24·4%). Unsolvated 4 : 4′-*dihydroxy*-3 : 3′-*dimethyl*-2″-*nitrotriphenylmethane* had m. p. 138—139°; crystals from aqueous alcohol retained a little solvent which was lost at 100°/3—5 mm. (Found : C, 72·1; H, 5·5; N, 4·0%; *M*, 352. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%; *M*, 349).

Condensation of Anisole and m-*Nitrobenzaldehyde.*—Condensations with 2 : 1 molar quantities, under varied conditions, yielded resins which failed to crystallize; crystallization could however be induced by seeding solutions of the resins with the compound which was readily prepared with excess of anisole, as follows. A solution of anisole (8·65 g., 4 mols.) and *m*-nitrobenzaldehyde (3·0 g., 1 mol.) in acetic acid (20 ml.) was cooled to 2°, and sulphuric acid (8 ml.) in acetic acid (12 ml.) was added dropwise. After a day the mixture had separated into two layers. It was kept for 4 days at 0° with occasional shaking, and then poured into ice–water. The oil was extracted with ether, and the solution washed with sodium hydroxide solution and dried ($CaCl_2$). Ether was removed, and the excess of anisole distilled off at 6—8 mm. The remaining viscous oil crystallized readily in unsolvated form from ethyl alcohol, methyl alcohol, light petroleum, or *cyclo*hexane. 4 : 4′-*Dimethoxy*-3″-*nitrotriphenylmethane*, large, stout prisms from light petroleum (b. p. 60—80°) (3·85 g., 55%), had m. p. 73—75° (Found : C, 72·0; H, 5·1; N, 4·0; OMe, 17·7%; *M*, 405. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0; OMe, 17·8%; *M*, 349). The same compound (m. p. and mixed m. p.) was prepared by methylating 4 : 4′-dihydroxy-3″-nitrotriphenylmethane with methyl sulphate and potassium hydroxide.

3-*Amino*-4′ : 4″-*dimethoxytriphenylmethane*. Ferrous sulphate and ammonia failed to reduce the nitro-compound, which was recovered. Acid reducing agents were also unsuccessful. The nitro-compound (1·05 g.) was reduced with hydrogen in ethyl alcoholic solution in the presence of Adams's catalyst (absorption 214 ml.; calc., 201 ml.). The product was an oil which was repeatedly extracted with hot 18% hydrochloric acid; the crystals of 3-*amino*-4′ : 4″-*dimethoxytriphenylmethane hydrochloride*, washed with 18% hydrochloric acid and dried, had m. p. *ca.* 120° (Found : C, 69·1; H, 6·3; N, 3·9; Cl, 10·0; OMe 16·8. $C_{21}H_{22}O_2NCl$ requires C, 70·9; H, 6·2; N, 3·9; Cl, 10·0; OMe, 17·4%).

No crystalline product was isolated from condensations of anisole with *o*- or *p*-nitrobenzaldehyde.

Condensation of 2 : 6-*Xylen*-1-*ol and* m-*Nitrobenzaldehyde.*—2 : 6-Xylen-1-ol (6·1 g.) and *m*-nitrobenzaldehyde (3·775 g.) were condensed as in the first example (time, 31 hr.). The product was a readily powdered solid, free from obvious resin, which by crystallization from light petroleum or aqueous alcohol yielded 4 : 4′-*dihydroxy*-3 : 5 : 3′ : 5′-*tetramethyl*-3″-*nitrotriphenylmethane* (8·0 g., 85%), m. p. 146°. The *benzene* compound crystallised in pale yellow rods which melted at *ca.* 100°, resolidified, and melted again at 146° (Found : loss at 116°/5 mm., 13·1. $3C_{23}H_{23}O_4N,2C_6H_6$ requires C_6H_6, 12·1%. Found for the desolvated compound : C, 73·1; H, 6·4; N, 3·7. $C_{23}H_{23}O_4N$ requires C, 73·2; H, 6·1; N, 3·7%). The p-*xylene* compound melted at 104°, resolidified, and melted again at 144—145° (Found : loss at 116°/5 mm., 15·5. $3C_{23}H_{23}O_4N,2C_8H_{10}$ requires C_8H_{10}, 15·8%). The *toluene* compound melted at *ca.* 100°, resolidified, and melted again at 143° (Found : loss at 116°/5 mm., 15·5. $3C_{23}H_{23}O_4N,2C_7H_8$ requires C_7H_8, 14·0%).

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The Catalysed Reactions of Simple Aromatic Compounds with Ethylenic Systems. Part III. Substituted Acrylic Acids.*

By J. F. J. Dippy and J. T. Young.

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The studies recorded in Part II * of this series have been extended to the behaviour of further substituted acrylic acids with benzene in the presence of anhydrous aluminium chloride as catalyst, and the results are presented in summarised form. Moreover, the reaction of phenylated aliphatic acids with chlorobenzene, a related problem, has been examined. An interpretation of the addition and replacement reactions is offered.

The first systematic examination of the reactions of unsaturated acids (including substituted cinnamic acids) with benzene under the influence of anhydrous aluminium chloride was by Eijkman (*Chem. Weekblad*, 1907, **4**, 727; 1908, **5**, 655). Addition of an aryl group fron the solvent to the ethylenic linkage was reported in most cases, and with αβ-unsaturated acids this occurred at the β-carbon, except in the cases of ββ-dimethyl- and α-phenyl-acrylic acids, where α-addition was claimed. It has since been shown (Hoffman, *J. Amer. Chem. Soc.*, 1929, **51**, 2542; Bergmann, Taubadel, and Weiss, *Ber.*, 1931, **64**, 1493) that the phenyl*iso*valeric acid obtained by Eijkman from ββ-dimethylacrylic acid is actually the product of β-aryl addition, and similar additions have since been demonstrated by Smith and Pritchard (*J. Amer. Chem. Soc.*, 1940, **62**, 771) with ψ-cumene, hemimellitene, *p*-xylene, and mesitylene ($AlCl_3$). In their experiment Bergmann *et al.* (*loc. cit.*) reported a second acid product, but using milder conditions we have obtained only a high yield of β-phenyl*iso*valeric acid (Expt. **1**, see Table).

On the other hand, Eijkman's claim of α-aryl addition in the reaction of α-phenylacrylic (atropic) acid with benzene has been confirmed by us, but only by using his experimental conditions (Expt. **4**); the slow reaction encountered here contrasts with the readiness of addition of benzene to the β-phenyl isomer (see Dippy and Young, *J.*, 1952, 1817). This is, therefore, the only substantiated instance of *α-aryl addition* in a reaction of this kind.

Addition of benzene to β-methyl-β-phenylacrylic acid to give ββ-diphenylbutyric acid in fair yield was reported by Bergmann, Taubadel, and Weiss (*loc. cit.*) using the conditions of Eijkman. In our experiment (Expt. 3), however, hydrogen transfer occurred chiefly, with some evidence of benzene addition (cf. the reaction of CPhMe=CH·COPh with benzene; Dippy and Palluel, *J.*, 1951, 1415); thus it appears that the dominating process here depends on the experimental conditions. It is noteworthy, also, that where *two* aryl groups occupy the β-position, hydrogen transfer occurs exclusively, ββ-diphenylpropionic acid thus being obtained in fair yield from ββ-diphenylacrylic acid (Expt. 2). A similar observation was made by Alexander, Jacoby, and Fuson (*J. Amer. Chem. Soc.*, 1935, **57**, 2208) who obtained ββ-diphenylpropionic acid on treating β-*p*-chlorophenylcinnamic acid with benzene ($AlCl_3$). This tendency to favour hydrogen transfer as the total bulk of the β-substituents increases may be interpreted in terms of steric hindrance, *i.e.*, the introduction of any other adduct than hydrogen is inhibited by a primary steric effect.

Fuson, Kozacik, and Eaton (*J. Amer. Chem. Soc.*, 1933, **55**, 3799) treated both *o*- and *p*-chlorocinnamic acid with benzene and chlorobenzene ($AlCl_3$) and recorded that, where benzene was used, the product was ββ-diphenylpropionic acid from both acids, whilst with chlorobenzene ββ-di-*p*-chlorophenylpropionic acid was obtained. With each of the chloro-substituted cinnamic acids, therefore, not only had the usual β-aryl additon occurred, but, also, the existing chlorophenyl group had been replaced by an aryl group supplied by the solvent; some confirmation of this was provided by Pfeiffer, Jenning, and Stöcker (*Annalen*, 1949, **563**, 73). The experiments of Fuson *et al.* (*loc. cit.*, 1933) represented the first examples of this type of replacement involving acids, although the general feature had previously been reported. Such reactions were designated by Fuson and his co-workers as

* Part II, *J.*, 1952, 1817.

the "reversible addition of an aromatic compound to a conjugated system" and this description has been used by later authors referring to this kind of process. To derive more information concerning the behaviour of acids of this type under such conditions, the reactions of *p*-methyl-, *p*-methoxy-, *o*-chloro-, and *m*-nitro-cinnamic acid with benzene ($AlCl_3$) have been examined by us; our aim, where possible, was to arrest the reactions at the addition stage.

Reactions of substituted acrylic acids with benzene.

Expt. no.	Unsaturated acid [1]	Reaction procedure [2]	Product	Yield (%)	Type of reaction
1	CMe_2=CH·CO_2H	(b)	CMe_2Ph·CH_2·CO_2H	94	β-Aryl addition
2	CPh_2=CH·CO_2H	(b)	$CHPh_2$·CH_2·CO_2H	55	Hydrogen transfer
3	CMePh=CH·CO_2H	(b)	CHMePh·CH_2·CO_2H (some evidence of $CMePh_2$·CH_2·CO_2H)	42	Principally hydrogen transfer
4	CH_2=CPh·CO_2H	[3]	$CMePh_2$·CO_2H	*ca.* 10	α-Aryl addition
5	,,	(a)	None	—	None
6	*p*-C_6H_4Me·CH=CH·CO_2H	(b)	$CHPh_2$·CH_2·CO_2H	75	β-Aryl addition with replacement
7	,,	(a)	$CHPh_2$·CH_2·CO_2H	100	
8	*o*-C_6H_4Cl·CH=CH·CO_2H	(a)	*cis*-*o*-C_6H_4Cl·CH=CH·CO_2H	38	*trans*–*cis*-Isomerisation
9	,,	(c)	*o*-C_6H_4Cl·CHPh·CH_2CO_2H	[6]	β-Aryl addition
10	,,	[4]	*o*-C_6H_4Cl·CHPh·CH_2CO_2H	18	
11	*p*-MeO·C_6H_4·CH=CH·CO_2H	(b)	*cis*-*p*-MeO·C_6H_4·CH=CH·CO_2H	[6]	*trans*–*cis*-Isomerisation
12	,,	(b) [5]	HO·C_6H_3Me·CHPh·CH_2·CO_2H	29	β-Aryl addition with isomeric rearrangement

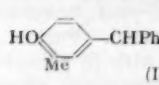
[1] All cinnamic acids were ordinary *trans*-modifications. [2] Reaction procedures (a), (b), (c), and (d) refer to experimental conditions established in Part II of this series. [3] Using the procedure of Eijkman (*loc. cit.*). [4] Using the procedure of Fuson, Kozacik, and Eaton (*J. Amer. Chem. Soc.*, 1933, **55**, 3799). [5] Larger proportion of catalyst. [6] High losses on recrystallisation.

The production of ββ-diphenylpropionic acid ("addition plus replacement" reaction) from *p*-methylcinnamic acid and benzene ($AlCl_3$) (Expts. 6 and 7) was in accordance with expectation since it compares with replacement of the *p*-tolyl group in an analogous unsaturated ketone (Eaton, Black, and Fuson, *J. Amer. Chem. Soc.*, 1934, **56**, 687); application of milder conditions (Expt. 7), however, failed to give the product of intermediate addition. It is noteworthy that whereas replacement of *p*-tolyl by phenyl is effected readily, replacement of phenyl by *p*-tolyl under the same experimental conditions (cf. Dippy and Young, *loc. cit.*) does not occur. Since the primary addition product is presumably the same in each case, this difference in behaviour seems to be a function of the two benzenoid solvents in the replacement process.

In the reaction between *o*-chlorocinnamic acid and benzene ($AlCl_3$), Fuson and his collaborators (*loc. cit.*, 1933) did not isolate an addition product, and, in our attempt to achieve this, under mild conditions [procedure (a), Expt. 8], *cis*-*o*-chlorocinnamic acid was produced (see Dippy, McGhie, and Young, *Chem. and Ind.*, 1952, 195). Nevertheless, the simple adduct, β-*o*-chlorophenyl-β-phenylpropionic acid was obtained by alternative procedures (Expts. 9 and 10); no replacement product arose in these experiments.

When *p*-methoxycinnamic acid was treated with benzene ($AlCl_3$) (Expt. 11), a solid separated on addition of the catalyst, from which a small quantity of a very labile acid, considered to be *cis*-*p*-methoxycinnamic acid, was isolated. The experiment was repeated with a higher proportion of catalyst (Expt. 12), and an acid was then recovered which was *not* identical with β-*p*-methoxyphenyl-β-phenylpropionic acid (obtained from anisole and cinnamic acid), although of the same m. p. and equivalent weight. From a consideration of the strength of this acid and those of acids of related constitution, the compound under review was assigned the constitution (I), a product of isomeric rearrangement. The following approximate values of dissociation constant (10^5K) were determined conductimetrically in water at 25°: Ph_2CH·CH_2·CO_2H, 3·2; *p*-MeO·C_6H_4·CHPh·CH_2·CO_2H, 3·0; the acid (I), 2·15. The low value in the last case excludes the possibility of there having

been α-aryl addition because the nearer is the situation of phenyl to carboxyl the stronger is the acid (cf. $Ph_2CH{\cdot}CO_2H$, $11{\cdot}15 \times 10^{-5}$); thus a ββ-diarylpropionic system is indicated for the acid (I). Moreover, it can be expected that *p*-hydroxyl will be more effective than *p*-methoxyl in depressing acid strength, and that the existence of *m*-methyl will reduce *K* still further (see Dippy, *Chem. Rev.*, 1939, **25**, 151).



(I)

With *m*-nitrocinnamic acid no reaction took place. Since in this case aluminium chloride separated as a complex with the acid, reaction was attempted with a large excess of catalyst, but without result.

The use of anhydrous stannic chloride and titanium tetrachloride as catalysts was explored with cinnamic acid and benzene as reactants to no effect, although aluminium bromide gave an excellent yield of ββ-diphenylpropionic acid.

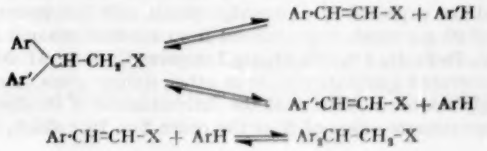
The mode of addition with substituted acrylic acids, as with αβ-unsaturated ketones (Dippy and Palluel, *loc. cit.*), is best regarded as nucleophilic attachment of the aromatic addendum to the carbon atom carrying the positive charge in a carbonium cation (III*a* or *b*) derived from the unsaturated acid under the influence of aluminium chloride. Normally this atom is the β-carbon in consequence of the polar character of carboxyl ($-I - M$). Nevertheless, one exceptional case of α-aryl attachment occurs, *viz.*, when atropic acid is used; this must be ascribed to the strong electron-release capacity ($+M$) of the phenyl group which at the α-position competes so effectively with the influence of carboxyl as to alter the polarity of the ethylene link. In other unsaturated acids under review phenyl, carried by the β-carbon, serves to augment the polarising influence of carboxyl; the β-carbon in such a case has therefore a relatively low electron density and so β-aryl orientation occurs, as the proposed mechanism (below) serves to ensure.

In the following scheme the promotion of a reactive cation is illustrated in terms of cinnamic acid (X represents the carboxyl group which has undergone reaction with aluminium chloride, an excess of which has been provided):

$$AlCl_4^- + \underset{(III b)}{Ph{\cdot}\overset{+}{C}H{\cdot}CH_2X} \xleftarrow{HCl} \underset{(II)\ AlCl_3^-}{Ph{\cdot}\overset{+}{C}H{\cdot}CHX} \xrightarrow{AlCl_3} \underset{(III a)\ AlCl_3}{Ph{\cdot}\overset{+}{C}H{\cdot}CHX} + AlCl_4^-$$

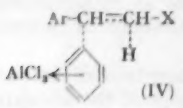
The use of hydrogen chloride as an alternative to aluminium chloride in the production of the cation from (II) is justified since hydrogen chloride is inevitably present during reaction. In the unique case of atropic acid the β-carbon atom becomes associated with the aluminium chloride, and here, therefore, the reactive centre of the eventual cation is the α-carbon atom.

The replacement reaction of the kind involved in the conversion of *p*-methylcinnamic acid into ββ-diphenylpropionic acid is not unusual. It was encountered in the reaction of cinnamic acid with chlorobenzene (Dippy and Young, *loc. cit.*) and by Fuson, Kozacik, and Eaton (*loc. cit.*) with chlorocinnamic acids and benzene. Probably the first case of this type of reaction was the conversion of ω-*p*-chlorobenzylidenequinalidine into 2-(2 : 2-diphenylethyl)quinoline by means of benzene and aluminium chloride (Hoffman, Farlow, and Fuson, *J. Amer. Chem. Soc.*, 1933, **55**, 2000). Other examples have since come to light involving unsaturated ketone, stilbene, and lepidine systems (Fuson *et al.*, *ibid.*, 1934, **56**, 687, 1241, 2103; 1936, **58**, 1979; Fuson and Cooke, *J. Amer. Chem. Soc.*, 1951, **73**, 3515; Dippy and Palluel, *loc. cit.*). It has been shown that in such reactions addition first occurs to give a saturated compound, followed by the slower replacement process, although so far only unsubstituted aryl (usually phenyl) or halogenophenyl groups have shown themselves capable of entering or of being withdrawn in this process (see Dippy and Young, *loc. cit.*). In all cases, a large excess of benzenoid solvent (ArH) is used, and this effects a favourable displacement of the following addition–elimination equilibria (first proposed by Fuson and his collaborators):



$$Ar{\cdot}CH{=}CH{-}X + ArH \rightleftharpoons Ar_2CH{-}CH_2{-}X$$

It is significant that we have been unable to observe exchange of aryl groups in the case of diphenylacetic acid and chlorobenzene, whereas, on the other hand, γγ-diphenyl-*n*-butyric acid in the same medium has yielded γγ-di-*p*-chlorophenyl-*n*-butyric acid. Further, replacement of the phenyl group by chlorophenyl could not be effected with (i) phenylacetic acid, (ii) deoxybenzoin, or (iii) β-phenylpropionic acid. These observations when added to the available information seem to imply that exchange occurs only with *gem*-diaryl groups and that these must occupy a position not less remote (from X) than the β-position. The need for a *gem*-diaryl system is possibly connected with the need for stabilisation of the ethylenic link (for which the residual aryl group provides) in the elimination process which, in the transition state (IV), might be represented as inset, where the electron-deficient $AlCl_3$ engages in a π-bond with an aryl group, the eventual withdrawal of which is effected, accompanied by loss of hydrogen (as proton) from the α-position. The replacement of aryl groups in γγ-diphenylbutyric acid might involve an elimination of proton from either α- or β-carbon atom, as the system is capable of three-carbon prototropy.



(IV)

Experimental

Reactions of Substituted Acrylic Acids with Benzene.—*ββ-Dimethylacrylic* (*3-methylbut-2-enoic*) *acid.* Procedure (b). ββ-Dimethylacrylic acid (20 g.), benzene (400 ml.), and aluminium chloride (50 g.) gave β-phenyl*iso*valeric acid (33·0 g.), m. p. 57—58° after recrystallisation from aqueous ethanol (Hoffman, *loc. cit.*, records m. p. 57·5—58·5°) (Found: equiv., 178. Calc. for $C_{11}H_{14}O_2$: equiv., 178) (anilide, m. p. 121°; Hoffman, *loc. cit.*, gives m. p. 122—123°).

β-Methyl-β-phenylacrylic (*3-phenylbut-2-enoic*) *acid.* Procedure (b). This acid (4 g.), benzene (100 ml.), and aluminium chloride (6 g.) yielded β-phenyl-*n*-butyric acid (1·7 g.), b. p. 142°/1 mm.; slow evaporation of a solution in light petroleum (b. p. 100—120°) gave crystals, m. p. 37° (Eijkman, *loc. cit.*, gives m. p. 37—38°, b. p. 140—145°/3 mm.) (Found: equiv., 165. Calc. for $C_{10}H_{12}O_2$: equiv., 164). A further acid fraction (0·3 g.), b. p. 180—190°/2 mm. (equiv., 193), could not be crystallised (probably β-phenyl-*n*-butyric acid mixed with some ββ-diphenyl-*n*-butyric acid).

ββ-Diphenylacrylic acid. Procedure (b). ββ-Diphenylacrylic acid (0·9 g.), benzene (10 ml.), and aluminium chloride (1 g.) yielded ββ-diphenylpropionic acid (0·5 g.), m. p. and mixed m. p. 156° (Pfeiffer and de Waal, *Annalen*, 1935, **520**, 185, give m. p. 154—155°).

α-Phenylacrylic acid (method of Eijkman, *loc. cit.*). α-Phenylacrylic acid (0·5 g.), benzene (3·3 ml.), and aluminium chloride (0·5 g., 1·1 mols. with respect to the acid) after 3 weeks gave a crude product (0·21 g.) from which αα-diphenylpropionic acid, m. p. 172°, was obtained by recrystallisation from aqueous ethanol [the structure of this acid has been fully established and the m. p. 173° recorded by Thörner and Zincke (*Ber.*, 1878, **11**, 1993), Bateman, and Marvel (*J. Amer. Chem. Soc.*, 1927, **49**, 2917), and Ziegler and Schnell (*Annalen*, 1924, **437**, 243)].

No reaction occurred by use of procedure (a).

p-*Methylcinnamic acid.* Procedure (b). *p*-Methylcinnamic acid (4 g.), benzene (100 ml.), and anhydrous aluminium chloride (6 g.) gave ββ-diphenylpropionic acid (4·2 g.), m. p. 156°. The same result was obtained with procedure (a).

o-*Chlorocinnamic acid.* Procedure (a). Ordinary *o*-chlorocinnamic acid (4·5 g.), benzene (90 ml.), and aluminium chloride (6 g.) gave *cis-o*-chlorocinnamic acid [recrystallised from benzene–light petroleum (b. p. 100—120°)], m. p. 128—129° (Stoermer *et al.*, *Ber.*, 1911, **44**, 637, record m. p. 127°) (1·7 g.) (Found: C, 59·8; H, 4·0; Cl, 19·4. Calc. for $C_9H_7O_2Cl$: C, 59·2; H, 3·9; Cl, 19·4%) (amide, m. p. 114°; Stoermer, *loc. cit.*, gives m. p. 112°). This acid decolorised cold aqueous alkaline potassium permanganate and produced an odour of aromatic aldehyde on warming. Exposure of a solution in acetic acid to ultraviolet light (*ca.* 20 hr.) raised the m. p. of the acid by 20—40°.

o-Chlorocinnamic acid (0·2 g.) and benzene by the method of Fuson, Kozacik, and Eaton (*loc. cit.*) did not yield the expected ββ-diphenylpropionic acid but instead β-o-*chlorophenyl-β-phenylpropionic acid* (0·05 g.) which recrystallised from aqueous ethanol in colourless needles, m. p. 133° (Found: C, 70·2; H, 5·0. $C_{15}H_{13}O_2Cl$ requires C, 69·1; H, 5·0%). (The presence of chlorine was demonstrated qualitatively, as in other similar cases described in this paper.) This acid is so sparingly soluble in water that the determination of its strength in this medium led only to a very approximate value of K of the order 2×10^{-5} which, however, suffices (on

comparison with the known data for reference acids in water) to demonstrate that both aryl groups are carried by the β-carbon atom.

Procedure (c), applied to the same quantities of reactants as in (a) above, gave crude β-*o*-chlorophenyl-β-phenylpropionic acid (5·5 g.) but recrystallisation losses were high.

p-*Methoxycinnamic acid.* Procedure (b). *p*-Methoxycinnamic acid (2·25 g.), benzene (55 ml.), and aluminium chloride (3 g.) were used. A bright yellow intermediate separated which remained after warming to 45° and stirring at intervals over 2 days at room temperature. The solid recovered after pouring on ice was treated with concentrated hydrochloric acid to give a pale-yellow viscous oil (2 g.) from which a somewhat pasty solid, m. p. 48—52°, was obtained after crystallisation from benzene–light petroleum (b. p. 60—80°) (Roth and Stoermer, *Ber.*, 1913, **46**, 260, give the m. p. of *cis-p*-methoxycinnamic acid as 66°). Slow evaporation of a solution in the same solvent during several weeks in ordinary light gave the normal *trans-p*-methoxycinnamic acid, m. p. and mixed m. p. 168°.

Procedure (b) was repeated, except that a much higher proportion of aluminium chloride was used. *p*-Methoxycinnamic acid (1·2 g.), benzene (40 ml.), and aluminium chloride (4·3 g., *ca.* 5 mols. with respect to the acid) gave a crude colourless product (0·5 g.) which on crystallisation twice from benzene–light petroleum (b. p. 100—120°) and twice from aqueous acetic acid gave colourless needles, m. p. 123° (10^5K, 2·15) to which the constitution β-4 -*hydroxy*-3-*methylphenyl*-β-*phenylpropionic acid* is assigned [admixed m. p. 96—106° with β-*p*-methoxyphenyl-β-phenylpropionic acid (Dippy and Young, *loc. cit.*), m. p. 122°; 10^5K, 3·0] (Found: C, 74·4; H, 6·3%; equiv., 256. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%; equiv., 256).

*Reaction between γγ-Diphenyl-*n*-butyric acid and Chlorobenzene.*—The procedure followed was that employed by Dippy and Young (*loc. cit.*) for the reaction between ββ-diphenylpropionic acid and chlorobenzene. From γγ-diphenylbutyric acid (2 g.), chlorobenzene (240 ml.), and aluminium chloride (11 g.) a yellow oil (2·6 g.) was obtained which on esterification gave *methyl γγ-di*-p-*chlorophenylbutyrate* (1·46 g.), a pale-yellow viscous liquid, b. p. 203—207°/5 mm. (Found: C, 63·7; H, 5·4. $C_{17}H_{16}O_2Cl_2$ requires C, 63·2; H, 5·0%). Direct fractional distillation of the crude acid product gave γγ-di-*p*-chlorophenylbutyric acid as an uncrystallisable pale-brown gum, b. p. 220—230°/3 mm.; oxidation of this with potassium permanganate yielded 4 : 4′-dichlorobenzophenone, m. p. 142—143° (Eaton, Black, and Fuson, *loc. cit.*, give 142—143°).

By a similar procedure (i) phenylacetic acid, (ii) diphenylacetic acid, (iii) β-phenylpropionic acid, and (iv) deoxybenzoin were treated, in turn, with chlorobenzene but no exchange of aryl groups was observed, *i.e.*, the starting material was recovered unchanged in each case.

The materials used in the course of this investigation were prepared by established methods except for the following, where adaptations were made.

ββ-*Diphenylacrylic Acid.*—Ethyl β-hydroxy-ββ-diphenylpropionate (5 g., 1 mol.), phosphoric oxide (3·28 g., 1·25 mol.), and benzene (15 ml.) were refluxed for 3 hr. (cf. Kon and Nargund, *J.*, 1932, 2461), whereupon ββ-diphenylacrylic acid was obtained (2·5 g.), having m. p. 161° (Rupe, *Annalen*, 1913, **395**, 136, reported m. p. 162°). Subsequent reduction with Raney nickel in aqueous alkali (cf. Papa, Schwenk, and Breiger, *J. Org. Chem.*, 1949, **14**, 366) gave ββ-diphenylpropionic acid, m. p. 156°.

γγ-*Diphenyl-*n*-butyric Acid.*—This was obtained by a Stobbe condensation. Diethyl succinate (13 g.), benzophenone (9·1 g.), and potassium *tert.*-butoxide gave a product which upon decarbethoxylation yielded a mixture of γγ-diphenylbutyrolactone and γγ-diphenylvinylacetic acid (Johnson, Petersen, and Schneider, *J. Amer. Chem. Soc.*, 1947, **69**, 74). To this, potassium iodide (1·03 g.) and red phosphorus (3 g.) were added, followed by phosphoric acid (*d* 1·75) (35 ml.) and water (5 ml.), and the mixture was refluxed for 6 hr. The whole was diluted with water and extracted with ether; the extract was washed with sodium hydrogen sulphite solution and water, and from it, after drying, pale brown crystals (9·3 g.) were recovered. These after recrystallisation from methanol and then light petroleum (b. p. 80—100°) gave γγ-diphenyl-*n*-butyric acid in colourless needles (4·7 g.), m. p. 105° (Ziegler, *Annalen*, 1929, **473**, 25, gives m. p. 105°) (Found: C, 79·9; H, 6·5%; equiv., 237. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·7%; equiv., 240). A much poorer yield was given by the Arndt–Eistert process.

We are indebted to Mr. J. W. Laxton and Mr. L. G. Bray for the measurement of the strengths of the acids reported here. These determinations were made by a conductivity method already described (*J.*, 1954, 1470) and results refer to aqueous solution at 25°.

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Palladium(0) *Compounds. Part I. Diisonitrilopalladium*(0) *Compounds.*

By Lamberto Malatesta.

[Reprint Order No. 6519.]

The preparation and properties of diamagnetic di*iso*nitrilopalladium(0) complexes, $(R{\cdot}NC)_2Pd^0$ ($R = C_6H_5$, p-C_6H_4Me, and p-$C_6H_4{\cdot}OMe$), are described. $(R{\cdot}NC)_2Pd^0$ reacts with one mole of iodine to give $(R{\cdot}NC)_2PdI_2$, and with triaryl phosphites to give $[(RO)_3P]_2(R{\cdot}NC)Pd$.

It is well known that, as the –NC group in *iso*nitriles possesses an electronic structure analogous to that of carbon monoxide, it is capable of forming co-ordination compounds of carbonyl type, with the central metal atom in a formally zero oxidation state.

The tetrakisaryl*iso*nitrilo-nickel compounds, $(Ar{\cdot}NC)_4Ni$, were first obtained by Hieber and Böckly (*Z. anorg. Chem.*, 1950, **262**, 344) and by Klages and Mönkemeyer (*Ber.*, 1952, **85**, 109) by the action of *iso*nitriles on nickel tetracarbonyl, and later by Malatesta and Sacco (*Accad. naz. Lincei, Rend. classe Sci. fis. mat. nat.*, 1951, **11**, 379) by direct reduction of nickel(II) salts in the presence of excess of *iso*nitrile. Also the nitrosyl*iso*nitrile compounds, $(NO)_2(R{\cdot}NC)_2Fe$, can be prepared by direct action of *iso*nitriles on the nitrosyl carbonyl $(NO)_2(CO)_2Fe$ as well as by treatment of Roussin's red or black salt with *iso*nitriles. They can be obtained even by addition of hydroxylamine to an alcoholic suspension of $(Ph{\cdot}NC)_4FeCl_2$ (*idem, Z. anorg. Chem.*, 1953, **273**, 247). Pure *iso*nitrile complexes of Group VIA metals (Cr, Mo, and W) cannot be obtained by the action of *iso*nitriles on the corresponding carbonyls; they are, however, obtained by reduction of suitable salts in the presence of excess of *iso*nitrile (see *idem, Ann. Chim., Italy*, 1953, **43**, 622, and previous reference quoted therein). Moreover Sacco (*Gazzetta*, 1953, **83**, 632) has shown that on treatment of dicobalt octacarbonyl with *iso*nitriles only compounds of the type $[(R{\cdot}NC)_6Co]^+[Co(CO)_4]^-$ are obtained.

The ability of *iso*nitriles to give remarkably stable zero-valent complexes, and the ease with which they are obtained by reduction of a suitable metal salt in the presence of excess of *iso*nitrile, prompted the author to attempt the preparation of zero-valent metal *iso*nitriles of metals whose pure carbonyls are not known. Of these, palladium appeared to be the most promising in view of its ability to form carbonyl and nitrosyl halides and the hitherto unknown di*iso*nitrilopalladium dihalides recently prepared in this department (Angoletta, *Ann. Chim. Italy*, in the press). By analogy with $(R{\cdot}NC)_4Ni$, the palladium(0) *iso*nitrile complex should be $(R{\cdot}NC)_4Pd$.

Attempts to prepare ions of the type $[(R{\cdot}NC)_4Pd]^{++}$ showed that they are unstable, and hence it was attempted to reduce the complex $(R{\cdot}NC)_2PdI_2$ in the presence of excess of *iso*nitrile, this complex being chosen owing to its ease of preparation. A large number of reducing agents were tried under widely different conditions, and finally a product of composition $(R{\cdot}NC)_2Pd$, and not the expected $(R{\cdot}NC)_4Pd$, was isolated.

The conditions under which reduction takes place are rather unusual. The compounds $(R{\cdot}NC)_2PdI_2$, which could not be reduced to the zero-valent state by strong reducing agents in acid, neutral, or slightly alkaline solution, are easily reduced in strongly alkaline solution (alcoholic potassium hydroxide) but only if more than 2 moles of *iso*nitrile per mole of $(R{\cdot}NC)_2PdI_2$ are present. In fact, if slightly less than 2 moles of *iso*nitrile are used not even traces of $(R{\cdot}NC)_2Pd$ are obtained, whereas a 5% excess over 2 moles results in a 50% yield. The reaction sequence can be represented as follows:

$$(1)\ (R{\cdot}NC)_2PdI_2 + 2R{\cdot}NC + 2KOH \longrightarrow [(R{\cdot}NC)_4Pd](OH)_2 + 2KI$$
$$(2)\ [(R{\cdot}NC)_4Pd](OH)_2 + R{\cdot}NC \longrightarrow (R{\cdot}NC)_4Pd + R{\cdot}NCO + H_2O$$
$$(3)\ (R{\cdot}NC)_4Pd \longrightarrow (R{\cdot}NC)_2Pd + 2R{\cdot}NC$$

The phenyl, p-tolyl, and p-methoxyphenyl compounds were prepared by this method. They are remarkably stable, and are precipitated from the reaction mixture in the pure state, in black-brown leaflets with metallic reflexes. They are diamagnetic, and practically

insoluble in all solvents. They dissolve in pyridine and nitrobenzene with complete decomposition.

The ratio *iso*nitrile : metal is 2 : 1 as shown by elementary analysis and by titration with an alcoholic iodine solution: reaction is quantitative according to $(R{\cdot}NC)_2Pd + I_2 \longrightarrow (R{\cdot}NC)_2PdI_2$.

On reaction with tervalent phosphorus derivatives, *e.g.*, tri-*p*-chlorophenyl phosphite, di*iso*nitrilopalladium(0) yields tetraco-ordinated palladium(0) complexes of the conventional type:

$$(R{\cdot}NC)_2Pd + 3(RO)_3P \longrightarrow [(RO)_3P]_3(R{\cdot}NC)Pd + R{\cdot}NC$$

Compounds of the latter type, which are now under investigation in these laboratories, constitute an important development in the complex chemistry of palladium.

The insolubility of the di*iso*nitrilopalladium(0) compounds suggests that they have a polymeric structure, and if so, this would be the first example of a polymeric *iso*nitrilo-complex.

It is well known that the pure carbonyls of Group VIIIA (Fe, Ru, and Os) and VIIIB (Co, Rh, and Ir) show a tendency to be more stable in the polynuclear form as the group is descended. Structural studies of polynuclear carbonyls, *e.g.*, $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$, show that the metal atoms are joined by bridging CO molecules acting as bidentate ligands, forming metal-to-carbon bonds of organometallic type.

If the carbon atom in the *iso*nitrile group were to function as a bidentate ligand, and this would be the first example of such a bond type, these palladium(0) complexes would form linear macromolecules in which *all* the bonds are of organometallic type. This seems highly improbable in view of the instability of organo-palladium compounds, the method of preparation of the palladium(0) *iso*nitriles, and their reaction with phosphites. Moreover, such a structure would leave palladium co-ordinatively unsaturated, as only four electrons would be donated to the central metal atom.

An alternative structure, with a co-ordinatively saturated palladium atom, could be envisaged as follows: each palladium atom forms four metallic bonds to other palladium atoms and two co-ordinate bonds to *iso*nitrile molecules. This would lead to a layer structure, with a monoatomic layer of palladium atoms sandwiched between *iso*nitrile molecule layers [something intermediate between the metal and the hypothetical $(R{\cdot}NC)_4Pd$], in which the central metal atom would have the effective atomic number of xenon.

The elucidation of the stereochemistry of these interesting compounds must, however, await an *X*-ray structure determination, and the author is prepared to supply samples to those interested in such a study.

Experimental

Palladium was determined as metal, carbon, and hydrogen by the Liebig method, and nitrogen by the Dumas method.

*Di(phenyliso**nitrilo**)palladium*(0), $(C_6H_5{\cdot}NC)_2Pd$.—Di(phenyl*iso*nitrilo)di-iodopalladium (1·13 g., 2 mol.) and phenyl*iso*nitrile (0·433 g., 4·1 mol.) in ethanol (15 ml.), in a 100-ml. flask, were heated to boiling and 20% alcoholic potassium hydroxide (1 ml.) was then added gradually. The clear, brownish-yellow solution obtained was again warmed to boiling and more alcoholic potassium hydroxide (3 ml.) added gradually. At this point a vigorous reaction set in: the solution became brown, then green, and finally green-brown, while dark brown leaflets begin to separate. After 15 min., reaction is complete and the solid is collected at the pump, washed with warm ethanol, cold water (to remove the residual KI), and then cold ethanol, and dried in a vacuum-desiccator [yield 0·4 g. (50%); decomp. 170—190°]. *Di(phenyliso**nitrilo**)palladium*(0) is diamagnetic ($\chi_M = -40 \times 10^{-6}$). It is insoluble in all solvents except *iso*nitriles, quinoline, pyridine, and nitrobenzene, but it cannot be recrystallised from these solvents (Found: C, 53·8; H, 3·3; N, 9·1; Pd, 34·3. $C_{14}H_{10}N_2Pd$ requires C, 53·75; H, 3·2; N, 9·0; Pd, 34·1%).

Reaction with iodine. The complex (0·310 g.) and alcoholic N/10-iodine (25 ml.) were shaken for 1 hr. and then titrated with N/10-thiosulphate; 5·3 ml. of solution were used, *i.e.*, 19·7 ml. of iodine [Calc. for reaction $(C_6H_5{\cdot}NC)_2Pd + I_2 \longrightarrow (C_6H_5{\cdot}NC)_2PdI_2$: 19·88 ml.]. The reaction product was collected (0·51 g., theor. 0·56 g.) and after recrystallisation proved to be identical with an authentic sample of $(C_6H_5{\cdot}NC)_2PdI_2$.

Di-(p-*tolylisonitrilo*)*palladium*(0).—This was prepared similarly in 55% yield from $(p\text{-}C_6H_4Me\cdot NC)_2PdI_2$ (1·1 g.) and *p*-tolylisonitrile (0·5 g.); decomp. 150—160° (Found: C, 56·0; H, 4·1; N, 8·1; Pd, 31·1. $C_{16}H_{12}N_2Pd$ requires C, 56·4; H, 4·1; N, 8·2; Pd, 31·6%). The *complex* (0·375 g.) and N/10-alcoholic iodine (25 ml.) were titrated as before and required 3·52 ml. of thiosulphate (calc., 3·00 ml.).

Di-(p-*methoxyphenylisonitrilo*)*palladium*(0).—By a similar method, this *complex* was obtained in 45% yield from $(p\text{-}MeO\cdot C_6H_4\cdot NC)_2PdI_2$ (1·25 g.) and *p*-methoxyphenylisonitrile (0·558 g.); decomp. 160—170° (Found: C, 51·5; H, 3·9; N, 7·3; Pd, 29·0. $C_{16}H_{12}O_2N_2Pd$ requires C, 51·3; H, 3·8; N, 7·5; Pd, 28·6%).

Reaction between $(C_6H_4Me\cdot NC)_2Pd$ *and Tri*-p-*chlorophenyl Phosphite*.—The complex (0·36 g., 1 mmole) and the ester (1·5 g., 4 mmoles) in benzene solution (3 ml.) were refluxed on a water-bath, until the dark solution become orange-yellow (about 10 min.). Benzene was then distilled off in a vacuum, and the dry residue washed twice with 5 ml. of cold absolute alcohol and crystallised from the same boiling solvent. p-*Tolylisonitrilotris*(*tri*-p-*chlorophenyl phosphite*) was thus obtained in white needles, m. p. 105° (sharp), which slowly blackened on exposure to air (Found: C, 51·0; N, 1·0; Cl, 22·3; P, 6·3; Pd, 7·4. $C_{62}H_{43}O_9NCl_9P_3Pd$ requires C, 50·8; N, 1·0; Cl, 21·9; P, 6·4; Pd, 7·3%).

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The Synthesis of Some N-*Substituted* 2-(3 : 4-*Dihydroxyphenyl*)*ethylamines.*

By E. J. Forbes.

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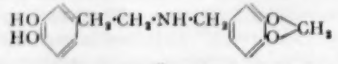
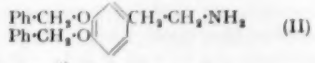
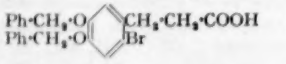
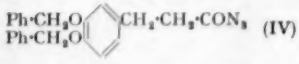
N-2-(3 : 4-Dihydroxyphenyl)ethyl-3 : 4-methylenedioxybenzylamine (I) has been synthesised with *O*-benzyl ethers as intermediates. *N*-(3 : 4-Dihydroxybenzyl)-2-(3 : 4-dihydroxyphenyl)ethylmethylamine (VII) has been prepared *via* its tetramethyl ether. In experiments relating to the synthesis of this tetramethyl ether, quaternary salts of Schiff's bases have been shown to undergo *N*-demethylation on catalytic reduction or treatment with lithium aluminium hydride.

N-Substituted 2-(3 : 4-dihydroxyphenyl)ethylamines (3 : 4-dihydroxyphenethylamines) were required for oxidation experiments, and this paper describes their preparation. The routes employed were determined by the nature of the substituents in the aromatic rings.

N-2-(3 : 4-Dihydroxyphenyl)ethyl-3 : 4-methylenedioxybenzylamine (I) and the *N*-(3 : 4-dihydroxybenzyl) analogue were prepared by Buck (*J. Amer. Chem. Soc.*, 1931, **53**, 2192) by demethylation of the corresponding methyl ethers. While this method was satisfactory for the latter substance, it proved unsuitable for obtaining the former in any reasonable quantity. This is not surprising since Späth and Quietensky (*Ber.*, 1927, **60**, 1882) found that when a methylenedioxy-group and vicinal methoxy-groups were present together, the former was hydrolysed preferentially.

(I)   (II)

(III)   (IV)

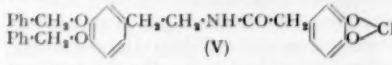
Since *O*-benzyl groups can readily be removed by hydrogenolysis, which leaves methylenedioxy-groups intact, we turned to the preparation of the dibenzyl ether of (I), with 2-(3 : 4-dibenzyloxyphenyl)ethylamine (II) as a preliminary.

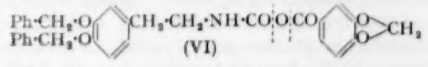
β-(3 : 4-Dibenzyloxyphenyl)propionic acid was prepared from the dihydroxy-acid, and its

amide was subjected to the Hofmann reaction, first, with sodium hypochlorite, which was without effect, and then in methanolic sodium methoxide with bromine. The latter procedure gave a monobromo-derivative of the amide, which was hydrolysed to the corresponding bromo-acid (probably III) and ammonia.

Methyl β-(3 : 4-dibenzyloxyphenyl)propionate was converted, *via* the hydrazide, into the azide (IV) (cf. Schöpf, Perrey, and Jächk, *Annalen*, 1932, **497**, 52). This decomposed smoothly in benzene to give 2-(3 : 4-dibenzyloxyphenyl)ethyl *iso*cyanate, which was subsequently hydrolysed, under acid and alkaline conditions, though the amine (II) was not obtained in either case. Acid hydrolysis removed also the benzyl groups, and alkaline conditions afforded the symmetrical urea.

Schöpf *et al.* (*loc. cit.*) obtained a high yield of the amide (V) from 2-(3 : 4-dibenzyloxyphenyl)ethyl *iso*cyanate and 3 : 4-methylenedioxyphenylacetic acid. When, in the present work, 3 : 4-methylenedioxybenzoic acid was used the expected amide was also obtained,


(V)

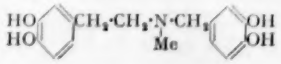

(VI)

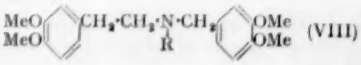
though the yield was so low (production of the urea and acid anhydride) that the route was not pursued further. The unwanted products may arise by disproportionation of the intermediate mixed anhydride (VI) at both of the positions indicated, followed by recombination of the appropriate fragments.

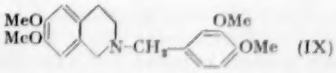
2-(3 : 4-Dibenzyloxyphenyl)ethylamine (II) was eventually obtained as its *N*-methoxycarbonyl derivative by decomposing the azide (IV) in boiling benzene containing methanol. The hydrolysis of the methoxycarbonyl compound with aqueous alcoholic alkali, to give 2-(3 : 4-dibenzyloxyphenyl)ethylamine (II), was unexpectedly easy. The amine (II) condensed readily with piperonaldehyde when heated, to give a Schiff's base, which was reduced catalytically to the dibenzyl ether of (I), in presence of a Raney nickel catalyst of only moderate activity. *O*-Debenzylation was accomplished by catalytically reducing the base hydrochloride in methanol at a palladium–barium sulphate catalyst. The product, *N*-2-(3 : 4-dihydroxyphenyl)ethyl-3 : 4-methylenedioxybenzylamine (I), was obtained in fine colourless needles (from propan-2-ol), m. p. 222°. Buck (*loc. cit.*) describes his product as a buff powder, m. p. 219°.

N-(3 : 4-Dihydroxybenzyl)-2-(3 : 4-dihydroxyphenyl)ethylmethylamine (VII) was obtained by demethylating its tetramethyl ether. During the preparation of this ether (VIII; R = Me) a number of unusual results were encountered.

Heating the secondary amine (VIII; R = H) with formaldehyde and formic acid gave a substance containing two hydrogen atoms less than the expected methylamine (VIII; R = Me). *O*-Demethylation furnished a substance which contained no *N*-methyl group and was again two hydrogen atoms short of the expected methylamine. The original product was then shown to be identical with 2-(3 : 4-dimethoxybenzyl)-1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxy*iso*quinoline (IX) obtained by the action of hydrochloric acid on the intermediate hydroxymethylamine.

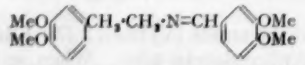
(VII) 

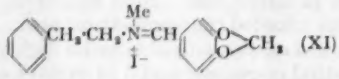

(VIII)


(IX)

Reduction of the quaternary methochloride of a 3 : 4-dihydro*iso*quinoline gave the corresponding tetrahydro-*N*-methyl*iso*quinoline (Späth and Hromatka, *Ber.*, 1929, **62**, 325). Likewise, the reduction of a quaternary salt of the Schiff's base 3 : 4-dimethoxybenzylidene-2-(3 : 4-dimethoxyphenyl)ethylamine (X) might be expected to give the required *N*-methylamine (VIII; R = Me) provided that hydrolytic conditions are avoided, as in catalytic reductions. In practice, the quaternary salt of the Schiff's base (X) dissolved in organic solvents only after addition of an appreciable amount of water, so reduction of

the azomethine group was usually forestalled by its hydrolysis, which gave 2-(3 : 4-dimethoxyphenyl)ethylmethylamine. When aqueous dioxan was used as the solvent, the amount of water present was a minimum (1—2%), and reduction of the azomethine group ensued, though the result was unexpected. Not only was the double bond reduced, but the *N*-methyl group was eliminated, giving the secondary amine *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylamine (VIII; R = H) obtained by reducing the Schiff's base (X). As far as the author is aware this is the only example known of the catalytic hydrogenolysis of an *N*-methyl group.

(X) 

 (XI)

A similar result was obtained when the closely related compound (XI) was treated with lithium aluminium hydride. When the dry solid methiodide (XI) was added to an ethereal solution of lithium aluminium hydride, a considerable evolution of gas accompanied dissolution of the yellow solid. From the resultant colourless solution the secondary amine *N*-(3 : 4-methylenedioxybenzyl)-2-phenylethylamine was isolated as the sole product. The reaction probably involves the initial elimination of the methyl group of the quaternary salt by a hydride ion, and in accordance with this view is the conversion of strychnine methosulphate into strychnidine with lithium aluminium hydride (Kenner and Murray, *J.*, 1949, S 178). This was considered to be an elimination reaction in which the methyl group, being more susceptible to S_N2 reactions than higher alkyl groups, was eliminated by a hydride ion (*idem*, *loc. cit.*). Both reactions may thus be formulated:

$$\equiv N^+—Me + H^- \longrightarrow \equiv N + CH_4$$

In the present case this would give a Schiff's base, which would be further reduced to a secondary amine. The use of the milder sodium borohydride in methanol (cf. Witkop and Patrick, *J. Amer. Chem. Soc.*, **1953**, **75**, 4474) gave mixtures which were not further investigated.

N-(3 : 4-Dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylmethylamine (VIII; R = Me) was obtained when 2-(3 : 4-dimethoxyphenyl)ethylmethylamine was condensed with 3 : 4-dimethoxybenzyl chloride in ethanol. It was more satisfactorily prepared by catalytic reductive alkylation of *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylamine (VIII; R = H). This elegant procedure was used by Tarbell and Craig (*J. Amer. Chem. Soc.*, 1948, **70**, 2783) to convert tetrahydropapaverine into laudanosine. The secondary amine (VIII; R = H) was treated with formaldehyde in ethanol, and the resulting hydroxymethylamine was hydrogenated at 3—4 atm. to the tertiary methylamine (VIII; R = Me) in 80% yield.

When heated with concentrated hydrochloric acid at 160—170°, the tertiary amine (VIII; R = Me) was smoothly demethylated to *N*-(3 : 4-dihydroxybenzyl)-2-(3 : 4-dihydroxyphenyl)ethylmethylamine (VII).

Experimental

2-(3 : 4-Dimethoxyphenyl)ethylamine was prepared by the hydrogenation of 3 : 4-dimethoxybenzyl cyanide in saturated alcoholic ammonia (Bide and Wilkinson, *Chem. and Ind.*, 1945, **64**, 84).

N-2-(3 : 4-*Dimethoxyphenyl*)*ethyl*-3 : 4-*methylenedioxybenzylamine*.—*N*-3 : 4-Methylenedioxybenzylidene-2-(3 : 4-dimethoxyphenyl)ethylamine (Buck, *loc. cit.*) (2·5 g.) was hydrogenated in dioxan (15 c.c.) at atmospheric pressure in presence of a fair quantity of Raney nickel. When reduction was complete (*ca.* 4 hr.), the liquid was filtered, the solvent was removed, and the residual amine was dissolved in dry ether. Treatment of the ethereal solution with dry hydrogen chloride precipitated the hydrochloride, needles, m. p. 200° (from dilute hydrochloric acid or ethanol) (Found: C, 61·6; H, 6·5; Cl, 10·0. Calc. for $C_{18}H_{22}O_4NCl$: C, 61·5; H, 6·3; Cl, 10·1%). Buck (*loc. cit.*) gives m. p. 219°. The *picrate* crystallised from aqueous ethanol in golden needles, m. p. 158° (Found: C, 52·9; H, 4·6; N, 10·2. $C_{24}H_{24}O_{11}N_4$ requires C, 52·9; H, 4·4; N, 10·3%).

β-(3 : 4-*Dibenzyloxyphenyl*)*propionic Acid*.—β-(3 : 4-Dihydroxyphenyl)propionic acid (36 g.)

(Schöpf, Perrey, Jächk, *Annalen*, 1932, **497**, 52), benzyl chloride (68·5 g.), and anhydrous potassium carbonate (82 g.) in absolute methanol (450 c.c.) were heated under reflux for 6 hr. The resulting benzyl ester was hydrolysed by heating it with potassium hydroxide (25 g.) in water (40 c.c.) for 4 hr. Most of the methanol was then removed, and water (1·2 l.) was added, giving a homogeneous solution which was extracted with ether and treated with charcoal. Acidifying the cooled solution gave the *acid* which crystallised from a small quantity of methanol in needles, m. p. 116—117° (52 g.). A second crystallisation afforded a specimen, m. p. 118° (Found : C, 76·3; H, 6·0. $C_{23}H_{22}O_4$ requires C, 76·2; H, 6·1%).

β-(3 : 4-*Dibenzyloxyphenyl*)*propionamide.*—β-(3 : 4-Dibenzyloxyphenyl)propionic acid (1 g.), thionyl chloride (1 c.c.), and chloroform (5 c.c.) were heated under reflux for 1 hr. Volatile material was removed under reduced pressure, and the residue was dissolved in a few c.c. of dioxan and poured into ice-cold concentrated ammonia. The precipitated *amide* crystallised from methanol in needles, m. p. 126° (Found : C, 76·2; H, 6·3; N, 4·1. $C_{23}H_{23}O_3N$ requires C, 76·2; H, 6·4; N, 3·9%).

Hofmann Reaction on β-(3 : 4-*Dibenzyloxyphenyl*)*propionamide.*—The amide (1·8 g.) and sodium methoxide (0·5 g.) were dissolved in warm methanol (30 c.c.). When bromine (0·3 c.c.) was added to the cooled solution its colour was immediately discharged. After being heated under reflux for 30 min., the solution was poured into water, giving a copious precipitate of an *amide*, which crystallised from methanol in small needles, m. p. 141—141·5° (Found : C, 62·4; H, 4·5; Br, 18·1. $C_{23}H_{22}O_3NBr$ requires C, 62·7; H, 5·0; Br, 18·2%).

This compound is polymorphic for on remelting it has m. p. 152—153°, undepressed on admixture with a specimen of the monobromide obtained as feathery needles, m. p. 153°, from benzene (Found : C, 63·0; H, 4·6; N, 3·4; Br, 18·3. $C_{23}H_{22}O_3NBr$ requires N, 3·2%).

When the amide was heated with aqueous-alcoholic alkali, ammonia was evolved. After 8 hr., the product was poured into water, and acidified. An oil, which soon solidified, was collected, dried, and taken up in hot benzene–light petroleum, which, on cooling, deposited the *acid* in needles, m. p. 116° (Found : C, 62·4; H, 4·9; Br, 18·2. $C_{23}H_{21}O_4Br$ requires C, 62·6; H, 4·8; Br, 18·1%).

β-(3 : 4-*Dibenzyloxyphenyl*)*propionhydrazide.*—β-(3 : 4-Dibenzyloxyphenyl)propionic acid (10 g.) was esterified in dioxan (30 c.c.) with ethereal diazomethane. Evaporation *in vacuo* left a gum which was heated with 90% hydrazine hydrate (10 c.c.) and pentyl alcohol (5 c.c.) under reflux for 5 hr., then allowed to cool. Overnight the solution deposited the hydrazide in colourless needles (8·3 g.), m. p. 138—139°.

β-(3 : 4-*Dibenzyloxyphenyl*)*propionazide and Its Rearrangement.*—(*a*) β-(3 : 4-Dibenzyloxyphenyl)propionhydrazide was converted into the azide by the method of Schöpf, Perrey, and Jächk (*loc. cit.*). The benzene solution of the azide, so obtained, was heated under reflux for 2 hr. By this time the evolution of nitrogen had ceased, and the benzene was removed by distillation. The residual *iso*cyanate was then heated under reflux for 4 hr. with aqueous-alcoholic alkali. On cooling and dilution with water, there was obtained a semi-solid product, which, after decantation of the alkali and washing with water, was obtained crystalline by trituration with ethanol. Recrystallisation from benzene or alcohol afforded the NN′-*di*-[2-(3 : 4-*dibenzyloxyphenyl*)*ethyl*]*urea* in needles, m. p. 168° (Found : C, 78·2; H, 6·5; N, 3·9. $C_{45}H_{44}O_5N_2$ requires C, 78·0; H, 6·4; N, 4·0%).

(*b*) A rigorously dried solution of the azide in benzene was heated under reflux for 2 hr., and a solution of 3 : 4-methylenedioxybenzoic acid in dioxan–benzene (dried azeotropically) was added. On cooling, the solution deposited crystals of the urea, m. p. and mixed m. p. 166—167°. Evaporation of the filtrate produced a precipitate of N-2-(3 : 4-*dibenzyloxyphenyl*)-*ethyl*-3 : 4-*methylenedioxybenzamide*, which crystallised from ethanol in needles, m. p. 136—137° (Found : C, 74·5; H, 5·7; N, 3·0. $C_{30}H_{27}O_5N$ requires C, 74·8; H, 5·6; N, 2·9%). Further evaporation of the solution produced a residue of 3 : 4-*methylenedioxybenzoic anhydride*, which crystallised from ethanol–benzene in needles, m. p. 147° (Found : C, 61·3; H, 3·2. $C_{16}H_{10}O_7$ requires C, 61·3; H, 3·2%).

(*c*) A rigorously dried solution of the azide in benzene (from 5·6 g. of hydrazide) was heated under reflux with methanol (50 c.c.) for 4 hr. After removal of the solvent, *methyl* N-2-(3 : 4-*dibenzyloxyphenyl*)*ethylcarbamate* remained as a solid, which crystallised from light petroleum containing a little benzene in needles (4·2 g., 75%), m. p. 78° (Found : C, 73·6; H, 6·5; N, 3·75. $C_{24}H_{25}O_4N$ requires C, 73·7; H, 6·4; N, 3·6%).

2-(3 : 4-*Dibenzyloxyphenyl*)*ethylamine* (II).—The foregoing ester (2 g.) was heated under reflux with aqueous-alcoholic potassium hydroxide for 8 hr. The cooled solution was diluted with water and the precipitated amine extracted with ether. When hydrogen chloride was

passed into the dried ethereal solution, 2-(3 : 4-*dibenzyloxyphenyl*)*ethylamine hydrochloride* was obtained as plates, m. p. 133° (1·5 g., 80%), which recrystallised from ethyl acetate containing a little ethanol (m. p. unchanged) (Found: C, 71·5; H, 6·8; N, 4·0; Cl, 9·5. $C_{22}H_{23}O_2N$,HCl requires C, 71·6; H, 6·5; N, 3·8; Cl, 9·5%).

2-(3 : 4-*Dibenzyloxyphenyl*)-N-3 : 4-*Methylenedioxybenzylidene-ethylamine*.—2-(3 : 4-Dibenzyloxyphenyl)ethylamine hydrochloride (1·2 g.) was suspended in water (10 c.c.), and just sufficient glacial acetic acid was added to render solution complete. Excess of alkali was then added and the precipitated amine extracted with chloroform (2 × 10 c.c.). The combined extracts were dried and the solvent was removed. Piperonaldehyde (0·5 g.) was added to the residual oil, and the mixture was heated at 100°/50 mm. for 30 min. By this time the water was removed, and the product was taken up in a large volume of hot ethanol, which, on cooling, deposited the *Schiff's base* (1·0 g.), needles, m. p. 77—78° (Found: C, 77·3; H, 6·1; N, 3·1. $C_{30}H_{27}O_4N$ requires C, 77·4; H, 5·8; N, 3·0%).

N-2-(3 : 4-*Dibenzyloxyphenyl*)*ethyl*-3 : 4-*methylenedioxybenzylamine*.—A solution of *N*-3 : 4-methylenedioxybenzylidene-2-(3 : 4-dibenzyloxyphenyl)ethylamine (2·0 g.) in dioxan (10 c.c.) was hydrogenated at atmospheric pressure with a Raney nickel catalyst of only moderate activity. After 1·5 hr., hydrogen uptake (1 mol.) was complete and the rate of adsorption had noticeably slackened. After filtration, the solution was evaporated, and water was added to the residue. The amine was extracted with ether and converted into its *hydrochloride* by hydrogen chloride. The salt crystallised from aqueous alcohol in needles (1·5 g.), m. p. 194° (Found: C, 71·5; H, 6·1; N, 2·7; Cl, 7·0. $C_{30}H_{29}O_4N$,HCl requires C, 71·8; H, 6·0; N, 2·8; Cl, 7·0%).

N-2-(3 : 4-*Dihydroxyphenyl*)*ethyl*-3 : 4-*methylenedioxybenzylamine*.—The foregoing hydrochloride (1·0 g.) in absolute methanol (100 c.c.) was hydrogenated at atmospheric pressure with a 5% palladium–barium sulphate catalyst (0·5 g.). When hydrogen uptake was complete (2 mols.) the catalyst was removed by centrifugation, thus avoiding prolonged exposure of the product to air. The solvent was then removed *in vacuo*, leaving a residue which was crystallised from propan-2-ol. *N*-2-(3 : 4-Dihydroxyphenyl)ethyl-3 : 4-methylenedioxybenzylamine hydrochloride was thus obtained as needles, m. p. 222° (Found: C, 59·3; H, 5·8; N, 4·4; Cl, 10·6. Calc. for $C_{16}H_{17}O_4N$,HCl: C, 59·4; H, 5·6; N, 4·3; Cl, 10·8%).

2-(3 : 4-*Dimethoxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dimethoxy*isoquinoline (X).—A mixture of *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylamine (5·0 g.), formic acid (3·8 c.c.), and 40% formaldehyde (1·8 c.c.) was heated on a steam-bath for 5 hr. On cooling, the mixture was rendered alkaline with 15% potassium hydroxide solution, giving a gum from which the aqueous layer was decanted. After being washed with water, the gum gave a white solid (2·5 g.) on trituration with ether. Extraction of the aqueous layer with chloroform gave a further quantity of base (0·5 g.). Two recrystallisations from ethanol afforded the isoquinoline in needles, m. p. 99° (Found: C, 69·7; H, 7·3. $C_{20}H_{25}O_4N$ requires C, 70·0; H, 7·3%).

The *methiodide* crystallised from aqueous methanol in needles, m. p. 222° (Found: I, 24·9. $C_{21}H_{28}O_4NI$,MeOH requires I, 24·6%), and the *picrate* from aqueous methanol in needles, m. p. 172° (Found: C, 54·2; H, 4·9; N, 9·6. $C_{26}H_{28}O_{11}N_4$ requires C, 54·5; H, 4·9; N, 9·8%).

2-(3 : 4-*Dihydroxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dihydroxy*isoquinoline.—A solution of the amine (IX) (1·0 g.) in colourless hydriodic acid (10 c.c.) was heated at 125° under carbon dioxide. After 30 min. the evolution of methyl iodide had ceased, and the solution was then evaporated to dryness. The residue was dissolved in water (15 c.c.), and the solution was neutralised with ammonia. The precipitated base was collected and rapidly transferred to water (10 c.c.), sufficient dilute hydrochloric acid being added to effect dissolution. Treatment of the decolorised solution with concentrated hydrochloric acid (1 c.c.) precipitated N-(3 : 4-*dihydroxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dihydroxy*isoquinoline *hydrochloride*, which crystallised from dilute hydrochloric acid in needles, m. p. 228° (Found, after drying *in vacuo* at room temperature: C, 56·2; H, 5·5. $C_{16}H_{18}O_4NCl,H_2O$ requires C, 56·3; H, 5·8%).

Cyclisation of N-(3 : 4-*Dimethoxybenzyl*)-N-2-(3 : 4-*dimethoxyphenyl*)*ethyl*-N-*hydroxymethylamine*.—The named compound was prepared by heating *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylamine (1 g.) and 40% formaldehyde (0·4 c.c.) on a steam-bath for 30 min. Water and excess of formaldehyde were then removed *in vacuo*, and 20% hydrochloric acid (4 c.c.) was added. After 1 hour's heating at 100° the solution was evaporated to dryness, giving a residue of 2-(3 : 4-dimethoxybenzyl)-1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxy*iso*quinoline hydrochloride, whose picrate and methiodide had m. p. and mixed m. p. 171—172° and 221—222°, respectively.

N-(3 : 4-*Dimethoxybenzyl*)-2-(3 : 4-*dimethoxyphenyl*)*ethyldimethylammonium Iodide*.—*N*-(3 : 4-Dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylamine (1·8 g.) and methyl iodide (2·0 c.c.) in

acetone (15 c.c.) were heated under reflux for 12 hr. Addition of water to the cooled solution produced a precipitate of the ***methiodide***, which crystallised from methanol in needles, m. p. 184° (Found : C, 52·0; H, 6·5. $C_{21}H_{30}O_4NI$ requires C, 51·8; H, 6·2%).

Quaternary Salts of 3 : 4-*Dimethoxybenzylidene*-2-(3 : 4-*dimethoxyphenyl*)*ethylamine* (X) *and their Catalytic Reduction.*—(*a*) A solution of the Schiff's base (2·0 g.) and acid-free methyl sulphate (0·8 g.) in dry benzene (20 c.c.) was heated for 15 min. at 100°. On cooling, the solution deposited a gum which solidified when triturated with ethanol. After two recrystallisations from ethanol, the ***methosulphate*** was obtained as stout needles, m. p. 170—171° (Found : C, 55·2; H, 6·6. $C_{21}H_{29}O_8NS$ requires C, 55·4; H, 6·4%).

A solution of the methosulphate (1·0 g.) in ethanol (50 c.c.) and water (10 c.c.) was hydrogenated at atmospheric pressure in presence of Adams catalyst (50 mg.) (2 hr.). The basic material was isolated in the usual manner, giving 2-(3 : 4-dimethoxyphenyl)ethylmethylamine. Its picrate and its hydriodide had m. p. and mixed m. p. 162—163° and 131° respectively.

(*b*) The methiodide of the Schiff's base (X) was prepared by the method of Späth and Hromatka (*Ber.*, 1929, **62**, 325). A solution of this salt (0·5 g.) in dioxan (60 c.c.) was hydrogenated at atmospheric pressure with Adams catalyst (50 mg.). By the time hydrogen uptake (32 c.c.) was complete (4 hr.), a crystalline precipitate had formed. After the addition of water (5 c.c.) to dissolve the precipitate, the solution was filtered and evaporated to dryness. By crystallising the residue from water, N-(3 : 4-*dimethoxybenzyl*)-2-(3 : 4-*dimethoxyphenyl*)-*ethylamine hydriodide* was obtained in needles, m. p. 206° (Found : C, 49·3; H, 5·8. $C_{19}H_{26}O_4NI$ requires C, 49·7; H, 5·7%). The N-*nitroso-compound* crystallised from ethanol in needles, m. p. 109—110° (Found : N, 7·7. $C_{19}H_{24}O_5N_2$ requires N, 7·8%).

The hydriodide and *N*-nitroso-compound were also prepared from the amine obtained by reducing the Schiff's base 3 : 4-dimethoxybenzylidene-2-(3 : 4-dimethoxyphenyl)ethylamine and had m. p. and mixed m. p. 206° and 109—110° respectively.

Reduction of N-3 : 4-*Methylenedioxybenzylidene*-2-*phenylethylmethylammonium Iodide with Lithium Aluminium Hydride.*—The methiodide was prepared essentially by the method of Robinson and Hamilton (*J.*, 1916, 1033). The reaction can be expedited by heating the components in a sealed tube at 100° for 1 hr. The crystalline methiodide so obtained, m. p. 85—87°, was used without further purification since, on crystallisation from ethanol, it undergoes some decomposition. It (2 g.) was added portionwise to an excess of lithium aluminium hydride in ether (5·6 c.c., diluted to 25 c.c.—1 c.c. of original solution was equivalent to 80 c.c. of hydrogen). The solid dissolved rapidly with much effervescence, giving a colourless solution. After decomposition of the mixture with dilute sulphuric acid, the organic layer was removed, and the aqueous layer was basified and extracted with ether. Dry hydrogen chloride was passed into the dried ethereal extract, affording a precipitate of N-(3 : 4-*methylenedioxybenzyl*)-2-*phenylethylamine hydrochloride* (1·0 g., 67%). It crystallised from dilute hydrochloric acid in needles, m. p. 250° undepressed on admixture with an authentic specimen (Found : C, 65·7; H, 6·5; Cl, 12·1. $C_{16}H_{17}O_2N,HCl$ requires C, 66·0; H, 6·2; Cl, 12·0%).

The ethereal solution, obtained when the reaction mixture was decomposed with dilute acid, yielded a small amount of non-ketonic material which was not investigated further.

When the reaction mixture was decomposed with alkali, instead of acid, basic material was removed from the ether with dilute acid. Treatment of the acid extract with sodium nitrite afforded the ***nitrosamine***, which was extracted with ether. Evaporation of the ethereal extract gave a gum, which solidified on trituration with ethanol. N-(3 : 4-*Methylenedioxybenzyl*)-N-*nitroso*-2-*phenylethylamine* crystallised from aqueous alcohol in fine colourless needles, m. p. 84° undepressed on admixture with an authentic specimen (Found : N, 9·7. $C_{16}H_{16}O_3N_2$ requires N, 9·9%).

Authentic specimens of the above hydrochloride and nitrosamine were prepared from the amine obtained by the catalytic reduction of 3 : 4-methylenedioxybenzylidene-2-phenylethylamine in dioxan with Raney nickel as catalyst.

Condensation of 2-(3 : 4-*Dimethoxyphenyl*)*ethylmethylamine with* 3 : 4-*Dimethoxybenzyl Chloride.*—2-(3 : 4-Dimethoxyphenyl)ethylmethylamine was prepared by decomposing the methiodide of the Schiff's base from 2-(3 : 4-dimethoxyphenyl)ethylamine and piperonaldehyde with water at 80°.

A solution of 2-(3 : 4-dimethoxyphenyl)ethylmethylamine (6·5 g.) and 3 : 4-dimethoxybenzyl chloride (5·1 g.) in absolute alcohol (20 c.c.) was set aside for 3 days. The dense crystalline precipitate which had formed was removed, washed with a little ethanol, dissolved in very dilute hydrochloric acid, and freed from secondary amine hydrochloride by treatment with sodium nitrite. After ether-extraction, the aqueous solution was basified and again extracted with

ether. The last ethereal extract was dried and treated with dry hydrogen chloride, giving a precipitate of N-(3 : 4-*dimethoxybenzyl*)-2-(3 : 4-*dimethoxyphenyl*)*ethylmethylamine hydrochloride* (3·2 g.), needles, m. p. 200° (from alcohol) (Found : C, 62·8; H, 7·4. $C_{20}H_{27}O_4N$,HCl requires C, 63·0; H, 7·3%). The corresponding *hydriodide*, prepared by treating the hydrochloride with sodium iodide in water, crystallised from water in needles, m. p. 187—188° (Found : C, 51·0; H, 5·9. $C_{20}H_{28}O_4NI$ requires C, 50·7; H, 5·9%).

Reductive Alkylation of N-(3 : 4-*Dimethoxybenzyl*)-2-(3 : 4-*dimethoxyphenyl*)*ethylamine.*—A solution of this amine (2 g.) and 40% formaldehyde (0·5 c.c.) in absolute ethanol (50 c.c.) was heated under reflux for 30 min. When the solution was cold, the hydroxymethyl compound was hydrogenated at 4 atm. at a Raney nickel catalyst (3 hr.). The solution was filtered and evaporated. The residual oil was freed from secondary amine with nitrous acid and converted into its hydrochloride (1·8 g., 80%), m. p. 200° alone and mixed with *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylmethylamine hydrochloride obtained previously. The *methiodide* crystallised from methanol in needles, m. p. 184° (Found : C, 52·0; H, 6·5. $C_{21}H_{30}O_4NI$ requires C, 51·8; H, 6·2%).

N-(3 : 4-*Dihydroxybenzyl*)-2-(3 : 4-*dihydroxyphenyl*)*ethylmethylamine.*—*N*-(3 : 4-Dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylmethylamine hydrochloride (2·5 g.) in concentrated hydrochloric acid (20 c.c.) was heated under carbon dioxide at 160—170° for 2 hr. The resultant colourless solution was evaporated to dryness *in vacuo*, leaving an almost colourless crystalline solid (Found : OMe, 0). This could not be recrystallised, nor could the hydriodide, both compounds being too deliquescent. The picrate was an amorphous solid.

To prove that the compound had undergone no further structural change during demethylation, it was dissolved in 33% potassium hydroxide and treated with methyl sulphate. Potassium iodide was then added, giving a precipitate of the methiodide, which after crystallisation from methanol had m. p. 184° alone and mixed with *N*-(3 : 4-dimethoxybenzyl)-2-(3 : 4-dimethoxyphenyl)ethylmethylamine methiodide.

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The Dyson Perrins Laboratory, Oxford. [*Received, June 20th*, 1955.]

The Preparation and Properties of Some Plutonium Compounds. Part I. Plutonium Hydride.

By F. Brown, Heather M. Ockenden, and G. A. Welch.

[Reprint Order No. 6452.]

Plutonium hydride with the approximate composition $PuH_{2\cdot7}$ has been obtained by direct combination of the metal with pure hydrogen at temperatures between 150° and 250°. Its chemical properties have been found to be very similar to those of the metal. By means of a thermobalance the hydride has been found to be stable in air up to 150°. *X*-Ray diffraction photographs showed two patterns, one of which was cubic and similar to that of plutonium dioxide, and the other hexagonal.

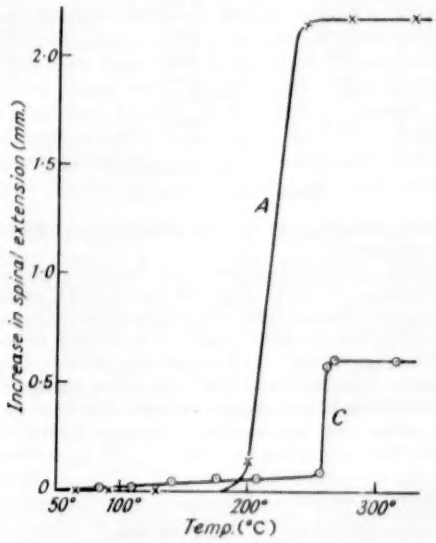
According to Burke (A.E.C.D. 2124, May 1944, declassified July, 1948) and Bakes and Johns (reported by Johns in L.A.D.C. 277, September 1944; M.D.D.C. 717, February 1947, declassified February 1947; reported by Kennedy and Smith L.A.M.S. 101, June 1944), plutonium and hydrogen react together at room temperature. Disintegration and powdering of the metal occur owing to the formation of a hydride. The method was to admit hydrogen slowly into an evacuated vessel containing plutonium and to measure the volume of hydrogen taken up. Burke (*loc. cit.*) reported three attempts, resulting in (*a*) no reaction, (*b*) $PuH_{2\cdot55}$ at 50°. (*c*) $PuH_{2\cdot75}$ at room temperature. Bakes and Johns (*locc. cit.*) in a more thorough investigation found the hydrogen to plutonium ratio by measuring the volume of hydrogen taken up and pumped off, several successive times, from samples of metal. They reported an average ratio (H/Pu) of 2·95 at 26·4°.

These workers published very few data on the chemical and physical properties of plutonium hydride and we have prepared and investigated it more fully.

Experimental

Preparation.—Bright plutonium metal (50—200 mg.) in a silica boat was placed in a silica combustion tube in a slow stream of dry oxygen-free (<1 p.p.m. of oxygen) hydrogen and the temperature of the sample was raised by means of an electric furnace until reaction occurred. Precautions were taken to prevent air from being sucked into the tube owing to rapid uptake of hydrogen. When the reaction was complete the hydride was allowed to cool in hydrogen.

In contrast to Burke, and to Bakes and Johns, we were unable to convert plutonium quantitatively into hydride at room temperature. A black coating formed on the outside of the metal and prevented any further action even after 16 hr. At temperatures between 150° and 200° darkening took place within about 30 min., then the metal rapidly disintegrated to coarse, black, still metallic-looking particles. In one case the sulphuric acid in the bubbler immediately following the combustion tube began to suck back for a few seconds owing to the sudden absorption of hydrogen. In several cases some particles of the hydride were projected out of the sample boat.



The reaction was followed more closely by heating plutonium in hydrogen on a thermobalance of silica-spring type similar to that described by Dawson, Elliott, Hurst, and Truswell (*J.*, 1954, 558). The increase in extension of the spring, which was measured by observing the movement of an index fibre by means of a cathetometer, was proportional to the increase in weight, the sensitivity being 0·909 mm./mg. The precision (3 × standard deviation) of any weighing at any temperature was calculated to be ±0·15 mm. or ±0·17 mg.

A platinum boat containing plutonium (about 40 mg.) was hung on the silica spring in hydrogen and the temperature was raised by about 30° every 15 min. Graph C in the Figure shows the increase in spiral length, plotted against temperature. It was believed that the sudden and complete increase in weight at 270° indicated that the point of reaction depended rather on an induction period than on temperature, especially since the hydride was normally prepared at a *lower* temperature.

Properties of Plutonium Hydride.—Appearance. The hydride was an almost black metallic-looking substance and appeared to occupy approximately the same volume as the original metal. It was hard, although grinding with a glass rod reduced it to a coarse powder with occasional sparking.

Action of water. In cold water there was no apparent reaction but on heating to 90°, a slow, steady flow of bubbles appeared and the solid partly broke down to a fine black oxide or hydroxide.

Action of mineral acids. In most respects plutonium hydride behaved very similarly to the

metal. It was virtually insoluble in 3M- or 16M-nitric acid, less than 10 μg. of plutonium per ml. of acid being dissolved even after prolonged heating. It dissolved readily with effervescence in hydrochloric acid (0·1—10M) and more slowly in sulphuric acid (3M) to give violet-coloured plutonium(III) salt solutions.

Hydrogen : plutonium ratio. This was determined by measuring the volume of hydrogen evolved on dissolving a known weight of hydride in 4N-hydrochloric acid. Corrections were made for temperature, pressure, water vapour pressure, and the volume of air displaced by the acid. Eight determinations on three different batches of plutonium hydride gave the results shown in the Table, the mean ratio being 2·69.

The hydrogen : plutonium ratio in plutonium hydride (calculated from the volume of hydrogen evolved with acid).

Sample	Mg.	Vol. of gas evolved (ml. at N.T.P.)	Ratios: H : hydride	H : Pu
Pu hydride (Batch No. 1)	33·8	8·83	5·66	2·67
	31·8	8·36	5·68	2·69
	34·5	9·18	5·75	2·76
	30·9	8·03	5·62	2·63
	34·7	9·15	5·70	2·71
Pu hydride (Batch No. 2)	32·7	8·48	5·61	2·62
	31·1	8·25	5·73	2·74
Pu hydride (Batch No. 3)	32·6	8·61	5·70	2·71
Pu metal	59·8	8·40 (2·99 equiv.)	—	—

Mean value = $PuH_{2\cdot69}$.

The apparatus was tested and found to be very satisfactory, 2·99 equiv. of hydrogen being obtained from pure plutonium metal.

Effects of air and heat. The hydride is fairly stable in air. In three weeks at room temperature, its weight only increased by 0·1% in dry air and by 1·3% in normal moist air. When heated in an open tube a sample glowed dully and changed into a greenish-yellow oxide. This oxidation was then followed on the thermobalance. It may be seen from the graph (curve *A*) that, when heated to 150° during 1½ hr., the hydride remained unchanged. Rapid oxidation then occurred, and further increase in temperature caused no change in weight. The product occupied several times the volume of the original hydride. A very similar curve was obtained with a second sample, B, except that the reaction was rather slower. The measurements were as follows :

	Sample A	Sample B
Extension due to hydride (mm.)	17·77	27·70
Maximum increase in extension (mm.)	2·19	3·25
Theoretical increase for the reaction $PuH_{3\cdot7} \longrightarrow PuO_2$ (mm.)	2·16	3·36

The deviations were only +0·03 mm., and −0·11 mm., both within the precision limits of the balance, *viz.*, ±0·15 mm.

Reaction with nitrogen. When the hydride was heated in nitrogen at 250°, a nitride, PuN, was formed. Its properties will be published in a subsequent paper.

Crystal structure. *X*-Ray diffraction photographs of a number of different samples of plutonium hydride (McDonald and Fardon, to be published) were essentially identical whether the sample had been exposed to air for only a few minutes, between preparation and photography, or for several days. A strong, face-centred cubic structure, very similar to that of plutonium dioxide, and a fainter hexagonal pattern were identified. Since the oxide content of the samples was known to be no more than 1—2% (see below) and there were small differences between this cubic structure and that found for PuO_2, the cubic phase was believed to be plutonium hydride. The hexagonal phase was too diffuse to be measured accurately but was attributed to about 5% of another hydride phase or an unidentified impurity. The density of the cubic phase was calculated to be 10·6 from *X*-ray data. This is considerably lower than the density of 19 reported for plutonium metal (Lord, *Nature*, 1954, **173**, 534; Ball, Robertson, Mardon, Lee, and Adams, *ibid.*, p. 535).

Discussion

The reaction between plutonium and hydrogen occurred at 100—200° after an induction period of 20—30 min. This was contrary to the results of Bakes and Johns (*locc. cit.*)

who found the reaction to take place at room temperature after an induction period of only a few minutes. Our observations show that plutonium behaves more like uranium (Katz and Rabinowitch, " The Chemistry of Uranium," McGraw Hill Book Co. Inc., New York, 1951, N.N.E S. VIII, Vol. 5), which reacts most rapidly with hydrogen at 250°. Uranium exhibits an induction period if the oxide layer is not removed from the surface of the metal or if the hydrogen is not rigorously freed from oxygen. It is probable that the induction period observed with plutonium was also due to the oxide film which forms immediately on the metal surface and is not easy to remove chemically.

As with uranium, the reaction, once it began, was completed rapidly. There was disintegration to a coarse dark powder and a slight increase in volume, but the change was small compared with that of uranium reacting under the same conditions to form a voluminous, fine, black powder.

The properties of plutonium hydride, particularly the reactions with air and mineral acids, were very similar to those of the metal.

The hydrogen to plutonium ratio was found to be 2·7. Bakes and Johns (*locc. cit.*) reported a value of 2·95, but, since the plutonium left after pumping off the hydrogen in their experiments would have been very finely divided and reactive, their results are not strictly comparable with those from massive metal. From the pressure–hydrogen-to-plutonium ratio isotherms they concluded that PuH_2 is formed, which in the presence of an excess of hydrogen reacts to give PuH_3 which remains in solid solution with the PuH_2. By extrapolation of these curves they predicted a ratio of about 3·0 at room temperature and 350 mm. pressure. Higher temperatures or lower pressures would give mixtures of PuH_2 and PuH_3.

The volume of hydrogen measured in our experiments was 5% lower than the amount required for a formula of PuH_3. There are four possible explanations for this low result :

(1) The hydride contained 5% of PuO or PuO_2, or other impurity which would not evolve hydrogen with hydrochloric acid. However, the amount of impurities in the original metal was very small and impurities formed during or immediately after preparation of the hydride were confined to oxides. The complete solubility of the hydride in dilute hydrochloric acid, the purity of the plutonium nitride resulting from the reaction with nitrogen, and the lack of plutonium monoxide lines in the *X*-ray diffraction patterns permit a limit of 1—2% to be given for these.

(2) The hydride contained 10% of unattacked plutonium metal which would liberate 3 equiv. of hydrogen instead of 6. This is unlikely since no plutonium metal pattern was detected in the *X*-ray diffraction photographs of the hydride, more prolonged heating in hydrogen caused no increase in the hydrogen to plutonium ratio, and hydride of smaller particle size did not give a higher ratio.

(3) The hydride consisted of a mixture of approximately 30% of PuH_2 and 70% of PuH_3. Two crystal structures were identified, one cubic and the other hexagonal, but only about 5% of the hexagonal phase was present. From Bakes and Johns's conclusions (*locc. cit.*) it seems likely that this mixture could occur although the PuH_2 should have been converted into PuH_3 on cooling in hydrogen.

(4) The hydride was a non-stoicheiometric compound. This is contrary to Bakes and Johns's theory of PuH_2 and PuH_3 in solid solution. However, examination of their isotherms reveals no proof of the existence of PuH_3 as a separate compound; they only show that hydrogen is being dissolved in PuH_2, forming a solid solution which appears to approximate in composition to PuH_3 under certain conditions. Therefore, if it is assumed that the solid solution was one of hydrogen in PuH_2, it is reasonable to suggest that plutonium hydride (H/Pu >2) is a non-stoicheiometric compound.

Plutonium hydride is obviously a member of the transitional-metal group of hydrides, having definite similarities with the hydrides of the rare earths, thorium, and uranium. Like them it has a considerably lower density than the metal, it is an exothermic, reactive compound with a crystal structure different from that of the metal, and has no simple stoicheiometric formula. Hurd (" Chemistry of the Hydrides," Chapman and Hall Ltd., London, 1952) has described how some transitional metals may form compounds with hydrogen and how the new structure formed physically absorbs more hydrogen. Zhukov

(*J. Russ. Phys. Chem. Soc.*, 1913, **45**, 2073) found evidence for the existence of CeH_2 from dissociation-pressure measurements. With higher hydrogen to cerium ratios the dissociation pressure of hydrogen was dependent upon the hydrogen content. The usual compound at atmospheric pressure is $CeH_{2\cdot69}$ (Hurd, *op. cit.*). This is analogous to the plutonium–hydrogen system. Other hydrides formed by the "lanthanide" and "actinide" elements are $PrH_{2\cdot84}$, Gd_2H_3, GdH_2, ThH_2, $ThH_{3\cdot4}$, PaH_3, UH_3, $NpH_{3\cdot7}$, and $AmH_{2\cdot7}$. The chemistry of these compounds has been reviewed by Hurd (*op. cit.*) and Seaborg and Katz ("The Actinide Elements," McGraw-Hill Book Co. Inc., New York, 1954). Rundle (*J. Amer. Chem. Soc.*, 1951, **73**, 4172) suggests that in uranium hydride the hydrogen atoms which lie in distorted tetrahedra, equidistant from four uranium atoms, are in holes which are larger than necessary and must result from the reaction. A similar observation has been made with ThH_2 (Rundle, Shull, and Wollan, *Acta Cryst.*, 1952, **5**, 22). This type of structure may occur in other similar hydrides, for example, plutonium hydride, where an exothermic reaction between the metal and hydrogen results in a change in crystal structure and an increased unit-cell volume. It is also possible that these reactions take place in two stages, the first giving the change of crystal structure, possibly resulting in a lower hydride, with a simple stoicheiometric formula, and the second being the expansion of the new structure by entry of more hydrogen atoms. The number of extra atoms added would depend upon the space available and on physical conditions such as temperature and pressure. This would give rise to the increased dissociation pressure with increased hydrogen content which has been observed with some transitional-metal hydrides and to their non-stoicheiometric formulæ.

All the *X*-ray work here recorded was carried out by B. J. McDonald and J. B. Fardon who will report their detailed results later. Their help is gratefully acknowledged. Thanks are offered to A.E.R.E., Harwell, for the silica spiral used in the thermobalance, and to J. K. Dawson of A.E.R.E. for full details of the construction of his balance. Thanks are also offered to the Managing Director of this Group for permission to publish this paper.

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Thermochemistry of Organophosphorus Compounds. Part I. Trimethyl and Triethyl Phosphites.

By C. L. Chernick, H. A. Skinner, and (in part) C. T. Mortimer.

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Values are reported for the heat of esterification of phosphorus trichloride by methanol and by ethanol in *cyclo*hexane. The heats of formation of the trialkyl phosphites are derived, *viz.*, $\Delta H_f^\circ[P(OMe)_3, liq.] = -175{\cdot}0$ and $\Delta H_f^\circ[P(OEt)_3, liq.] = -204{\cdot}1$ kcal./mole.

The mean bond dissociation energies, $\bar{D}$(P–OR), are calculated to lie within the range 79—82 kcal./mole.

Neale and Williams (*J.*, 1955, 2485) recently studied the thermochemistry of some organophosphorus compounds, making extensive use of reaction calorimetry. We have made similar studies, and acknowledge the advice and assistance given us (from their prior experience) by Neale and Williams. In this paper we report some measurements on the heats of reaction of phosphorus trichloride with methanol, and with ethanol, using essentially the experimental procedure employed by Neale and Williams in their studies of phosphorus trichloride–alcohol reactions. Our value for the heat of formation (ΔH_f°) of triethyl phosphite agrees closely with that given by Neale and Williams; a value for trimethyl phosphite has not previously been given.

Experimental

Compounds.—Commercial phosphorus trichloride was fractionally distilled in dry nitrogen, and finally in a vacuum into glass ampoules which were then sealed. *cyclo*Hexane (spectroscopic grade) was dried over sodium, and dimethylaniline ("AnalaR") over potassium hydroxide pellets. Ethanol was clinical-grade absolute, and methanol a high-quality synthetic product. Triethyl phosphite was prepared by Ford-Moore and Perry's method (*Org. Synth.*, 1951, **31**, 111), and purified by fractional distillation under reduced (nitrogen) pressure through an 8" gauze-packed column; it had b. p. 54·3—54·8°/15 mm.

Calorimeter.—The calorimeter was described by Mortimer and Skinner (*J.*, 1952, 4331). The esterifications were carried out in the Dewar vessel by breaking ampoules containing known weights of phosphorus trichloride under the surface of 750 c.c. of *cyclo*hexane, to which known amounts of alcohol and dimethylaniline had been added. The ensuing temperature changes were followed through the change in resistance of a shielded thermistor element immersed in the solution. The calorimeter was calibrated electrically by the substitution method.

Units.—All heat quantities are given in units of the thermochemical calorie, 1 cal. ≡ 4·1840 abs. joule. The reactions were carried out at 25°.

Results.—The observed heats of reaction ($\Delta H_{obs.}$) refer to the equation:

$$PCl_3\ (liq.) + \{n\text{ROH} + n\text{Ph·NMe}_2\}\ (\textit{cyclo}\text{hexane soln.}) \longrightarrow \{P(OR)_3 + (n-3)\text{ROH} + (n-3)\text{Ph·NMe}_2\}\ (\text{soln.}) + 3\text{Ph·NMe}_2\text{HCl (cryst.)} \quad . \quad (1)$$

where R = Me or Et. For the reactions with ethanol, values of n ranging from 3·3 to 8·0 were used, although in most experiments n was 4·0. For the reactions with methanol, n was 4·0 throughout. The reaction times, with $n = 4$ (or larger), varied somewhat but were generally less than an hour. Reaction to completion was appreciably slower for n values less than 4.

Esterification by Ethanol.—A selection of values of $\Delta H_{obs.}$ for the ethanol–phosphorus trichloride reaction is given in Table 1. The decrease in $\Delta H_{obs.}$ for values of $n > 4$ is a consequence of the dependence of the heat of solution of ethanol in *cyclo*hexane on the relative concentrations of the components. Values of the heat of solution of ethanol in ethanol–*cyclo*hexane solutions were measured separately, and are given in Table 2. The heats of solution in *cyclo*hexane of dimethylaniline and triethyl phosphite were also measured independently, and found to be 1·60 and 1·32 kcal./mole, respectively. For the derivation of $\Delta H_f^\circ[P(OEt)_3, \text{liq.}]$, it is useful to use the $\Delta H_{corr.}$ values given in the final column of Table 1; these are obtained from $\Delta H_{obs.}$ on removal of all those heat terms due to the use of *cyclo*hexane solvent, so that $\Delta H_{corr.}$ is the heat of the idealised reaction:

$$PCl_3\ (liq.) + 3\text{EtOH (liq.)} + 3\text{Ph·NMe}_2\ (liq.) \longrightarrow P(OEt)_3\ (liq.) + 3\text{Ph·NMe}_2\text{HCl (cryst.)} \quad . \quad (2)$$

Table 1. *Reaction of* PCl_3 *with excess of ethanol.*

PCl_3 (g.)	n (eqn. 1)	$-\Delta H_{obs.}$ (kcal./mole)	$-\Delta H_{corr.}$	PCl_3 (g.)	n (eqn. 1)	$-\Delta H_{obs.}$ (kcal./mole)	$-\Delta H_{corr.}$
0·6572	4·0	95·0	74·3	0·6313	5·0	95·2	75·3
0·6323	4·0	94·9	74·2	0·6198	7·0	92·7	74·7
0·6991	4·0	95·3	74·6	0·6286	8·0	92·1	76·1

Mean $\Delta H_{corr.} = -74·8$ kcal./mole.

Table 2. *Heat of solution of* EtOH *in* cyclo*hexane–ethanol.*

EtOH added (g.)	EtOH present initially (g.)	Ratio initial : finish EtOH	ΔH mixing (kcal./mole of added EtOH)	EtOH added (g.)	EtOH present initially (g.)	Ratio initial : final EtOH	ΔH mixing (kcal./mole of added EtOH)
0·6351	0·21	1 : 4	5·73	0·6276	0·84	4 : 7	4·83
0·6428	0·42	2 : 5	5·47	0·6671	1·11	5 : 8	4·19
0·6232	0·53	2·5 : 5·5	5·25	0·6337	1·16	5·5 : 8·5	4·18
0·6376	0·64	3 : 6	5·01				

Esterification by Methanol.—A selection from the observed heats of reaction is given in Table 3. In these reactions, the amount of alcohol used was adjusted to $n = 4·0$ (eqn. 1) in all cases. The heat of solution of methanol in methanol–*cyclo*hexane for this concentration range was measured separately: ΔH_{mixing} (1 : 4) = 5·70 kcal. per mole of MeOH added. The heat of solution of trimethyl phosphite in *cyclo*hexane is assumed to be the same as that measured for triethyl phosphite.

TABLE 3. *Reaction of* PCl_3 *with excess of methanol.*

PCl_3 (g.)	n (eqn. 1)	$-\Delta H_{obs.}$ (kcal./mole)	$-\Delta H_{corr.}$ (kcal./mole)	PCl_3 (g.)	n (eqn. 1)	$-\Delta H_{obs.}$ (kcal./mole)	$-\Delta H_{corr.}$ (kcal./mole)
0·6898	4·0	94·05	73·45	0·7663	4·0	95·15	74·55
0·6399	,,	94·2	73·6	0·6335	,,	95·0	74·4
0·6390	,,	93·6	73·0	0·6124	,,	93·5	72·9

Mean $\Delta H_{corr.} = -73{\cdot}7$ kcal./mole.

Heats of Formation.—The heats of formation of the alkyl phosphites are related to the corresponding $\Delta H_{corr.}$ through the thermochemical equation :

$$\Delta H_f^\circ[P(OR)_3, \text{liq.}] = \Delta H_{corr.} + \Delta H_f^\circ(PCl_3, \text{liq.}) + 3\Delta H_f^\circ(ROH, \text{liq.}) + 3\{\Delta H_f^\circ(Ph{\cdot}NMe_2, \text{liq.}) - \Delta H_f^\circ(Ph{\cdot}NMe_2HCl, \text{cryst.})\} \quad . \quad . \quad (3)$$

The *difference* $\Delta H_f^\circ(Ph{\cdot}NMe_2, \text{liq.}) - \Delta H_f^\circ(Ph{\cdot}NMe_2HCl, \text{cryst.})$ was measured in the following manner. Dimethylaniline was dissolved in excess of N-hydrochloric acid :

$$Ph{\cdot}NMe_2 \text{ (liq.)} + HCl,54H_2O + \text{excess of acid solution} \longrightarrow Ph{\cdot}NMe_2,HCl \text{ in acid solution}$$
$$\Delta H = -6{\cdot}54 \pm 0{\cdot}1 \text{ kcal./mole}$$

The heat of solution of crystalline dimethylaniline hydrochloride in excess of N-hydrochloric acid was also measured directly :

$$Ph{\cdot}NMe_2,HCl(\text{cryst.}) + \text{excess of acid solution} \longrightarrow Ph{\cdot}NMe_2,HCl \text{ in acid solution.}$$
$$\Delta H = 1{\cdot}93 \pm 0{\cdot}05 \text{ kcal./mole}$$

Whence, using $\Delta H_f^\circ(HCl,54H_2O) = -39{\cdot}60$ kcal./mole (Nat. Bur. Stand. Tables, Circular 500), we derive for the difference required, $48{\cdot}07 \pm 0{\cdot}08$ kcal./mole. Of the remaining terms in eqn. (3), $\Delta H_f^\circ(EtOH, \text{liq.}) = -66{\cdot}36$ kcal./mole and $\Delta H_f^\circ(MeOH, \text{liq.}) = -57{\cdot}04$ kcal./mole are well-established (*op. cit.*) : the value $\Delta H_f^\circ(PCl_3, \text{liq.}) = -74{\cdot}4$ kcal./mole, recently obtained by Neale and Williams (*J.*, 1954, 2156), is accepted here. Accordingly, from the mean $\Delta H_{corr.}$ values in Tables 1 and 3, and eqn. (3), we derive : $\Delta H_f^\circ[P(OMe)_3, \text{liq.}] = -175{\cdot}0$ kcal./mole, and $\Delta H_f^\circ[P(OEt)_3, \text{liq.}] = -204{\cdot}1$ kcal./mole. The absolute limits of error to be attached to these values are difficult to assess, since the accepted value for $\Delta H_f^\circ(PCl_3, \text{liq.})$ is itself subject to possible error latent in the heat of formation of phosphoric acid. The experimental errors in our $\Delta H_{corr.}$ values we would assess at *ca.* ± 1 kcal./mole.

Discussion.—The value of $\Delta H_f^\circ[P(OEt)_3, \text{liq.}]$ reported here is in good agreement (within the error limits of the individual determinations) with that given by Neale and Williams (*loc. cit.*). It may also be remarked that the *difference* between the heats of formation of liquid trimethyl phosphite and triethyl phosphite (29·1 kcal./mole) is of similar magnitude to the difference between the heats of formation of liquid trimethyl and triethyl arsenites (27·5 kcal./mole; Charnley, Mortimer, and Skinner, *J.*, 1953, 1181), and between the heats of formation of liquid trimethyl and triethyl borates (27·3 kcal./mole; Charnley, Skinner, and Smith, *J.*, 1952, 2288).

The mean bond dissociation energies $\bar{D}$(P–OR) [defined as one-third of the heat required to dissociate one mole of gaseous $P(OR)_3$ into gaseous P atoms and ·OR *radicals*] may be calculated from the heats of formation, in conjunction with the following subsidiary thermal data : $\Delta H_f^\circ(P, \text{g.}) = 75{\cdot}2$ kcal./mole (*op. cit.*), $\Delta H_f^\circ(\cdot OMe, \text{g.}) = -1{\cdot}3 \pm 2$ kcal./mole, $\Delta H_f^\circ(\cdot OEt, \text{g.}) = -8{\cdot}1 \pm 1$ kcal./mole (Charnley, Mortimer, and Skinner, *loc. cit.*), and $\Delta H_{vap.}[P(OMe)_3] = 8{\cdot}8$ kcal./mole, $\Delta H_{vap.}[P(OEt)_3] = 10{\cdot}0$ kcal./mole (estimated from vapour-pressure data in the literature). We obtain $\bar{D}$(P–OMe) = 79·2 and $\bar{D}$(P–OEt) = 81·7 kcal./mole. Gray (*Proc. Roy. Soc.*, 1954, **221**, *A*, 462) has recently given slightly different values from the above for the heats of formation of ·OMe and ·OEt radicals, *viz.*, $\Delta H_f^\circ(\cdot OMe, \text{g.}) = -0{\cdot}5$ and $\Delta H_f^\circ(\cdot OEt, \text{g.}) = -9{\cdot}0$ kcal./mole. With these values we obtain 80·0 and 80·8 kcal./mole, respectively, for $\bar{D}$(P–OMe) and $\bar{D}$(P–OEt).

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The Oxides of Uranium. Part VI. The Chemisorption of Reducing Gases on Uranium and Thorium Dioxides.*

By L. E. J. Roberts.

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Carbon monoxide is chemisorbed by uranium dioxide and by thoria at temperatures below 20°. There is mutual interference between the adsorption of oxygen and carbon monoxide on uranium dioxide at low temperatures. The adsorption of carbon monoxide by uranium dioxide at higher temperatures is small. Hydrogen is not appreciably chemisorbed by uranium dioxide below 400°, but at higher temperatures an activated adsorption occurs and high surface coverages can be attained. The results are discussed in terms of the numbers and the nature of the adsorption sites available.

Uranium dioxide adsorbs oxygen at −183°; a large fraction of the available surface is covered by a chemisorbed layer, about 75% of which is stable at temperatures up to room temperature (Part V *). Additional oxygen is adsorbed into the uranium dioxide lattice at temperatures above −80°, and the final result of oxidation is the production of interstitial anions. This type of chemisorption is different from the activated adsorption of oxygen on other oxidisable oxides such as cuprous oxide, where oxidation leads to the production of cation vacancies (Garner, Stone, and Tiley, *Proc. Roy. Soc.*, 1952, *A*, **211**, 472). The adsorption of carbon monoxide and of hydrogen on uranium dioxide provides further comparisons with chemisorption phenomena on other oxides. In addition, the effect of adsorbed carbon monoxide and hydrogen on adsorption of oxygen by uranium dioxide, and the effect of adsorption of oxygen on the subsequent adsorption of carbon monoxide yield information about the nature of the adsorbing centres in each case. The adsorption of carbon monoxide on thoria was also studied in order to obtain comparable data on adsorption of carbon monoxide on an oxide of the same structure as uranium dioxide but which is inert to oxygen and in which the cations cannot easily change their valency.

Experimental

The adsorption apparatus used for the bulk of this work was the constant-volume, variable-pressure apparatus described in Part V (*loc. cit.*). Some experiments were also performed in a constant-pressure, variable-volume apparatus. Desorbed gases were analysed for carbon dioxide and water by passing them through a U-tube cooled to −183° or −80°, and subsequently allowing any condensed material to expand into an evacuated volume where the pressure could be determined, a manometer filled with Apiezon "A" oil being used.

The details of the preparation of the various samples of uranium dioxide are given in Part V, together with their density, mean particle size, and mean crystallite size. The samples used in this work were B1 and C3, prepared by reduction of higher oxides with hydrogen and with carbon monoxide respectively, and R, prepared by heating a pure commercial dioxide to 2200° in a vacuum, crushing the sintered mass, and then treating it with hydrogen. These were all well crystallised samples with particle diameter of 0·45, 0·41, and 2·3 μ, respectively.

Thoria was prepared from a pure sample of the carbonate, supplied by Thorium Limited, by heating it in air to 1000° and in vacuum to 2000°, and crushing it.

Results

Adsorption of Carbon Monoxide by Uranium Dioxide.—Curves I and II of Fig. 1 are adsorption isotherms at −183° of carbon monoxide on uranium dioxide samples B1 and C3. Sample B1 had been treated with hydrogen at 700° and pumped at 740°; sample C3 had been reduced with carbon monoxide at 700° and pumped at 750°. The amounts adsorbed are expressed as V/V_m, V being the volume of gas adsorbed and V_m (both in c.c. at N.T.P.) the quantity of oxygen required to form a monolayer of physically adsorbed oxygen at −183°, as calculated by

* Part V, *J.*, 1954, 3332.

applying the B.E.T. equation to the physical adsorption of oxygen on these samples after low-temperature oxidation (Part V). After the determination of the carbon monoxide isotherms at −183°, the samples were pumped at −183° for 1 hr., by which time the rate of gas evolution was immeasurably small, and the isotherms redetermined at −183°; the results are plotted as curve III in Fig. 1. Curve III is parallel to the isotherms determined on a clean surface, but uniformly lower. If the carbon monoxide was removed at higher temperatures, at −120° or −80°, and the isotherm redetermined at −183°, parallel curves intermediate between curves I and II were obtained. Pumping at 250° removed all adsorbed carbon monoxide and the original isotherms, I or II, could be accurately reproduced.

Curve IV of Fig. 1 is a typical isotherm of physically adsorbed oxygen on an oxidised surface of uranium dioxide; curve IV is quite different in shape from curves I, II, or III, particularly

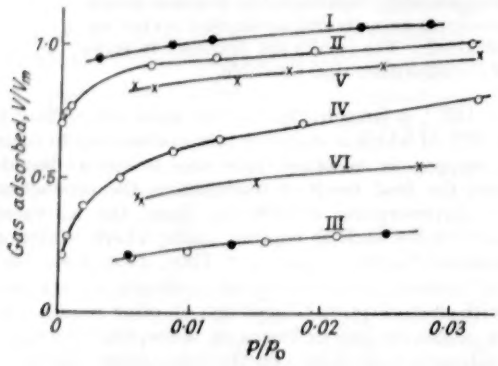

FIG. 1. *The adsorption of carbon monoxide and of oxygen on uranium dioxide at* −183°.

Curves I and II—carbon monoxide adsorption on reduced uranium dioxide; III—repeats of I and II after pumping at −183°; V—carbon monoxide adsorption on oxidised uranium dioxide; VI—repeat of V after pumping at −183°; IV—physical adsorption of oxygen on oxidised uranium dioxide.

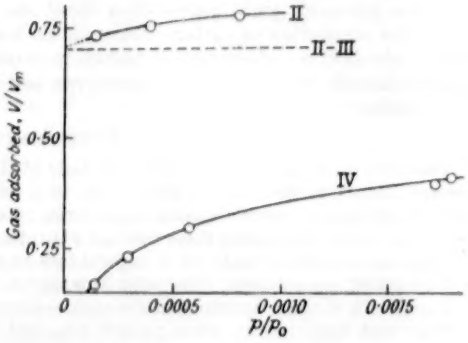

FIG. 2. *The adsorption of carbon monoxide and of oxygen at low pressures by uranium dioxide at* −183°.

Curve II—carbon monoxide adsorption on reduced uranium dioxide; IV—physical adsorption of oxygen on oxidised uranium dioxide; II—III—by subtraction of curves in Fig. 1.

at low pressures. This point is further illustrated in Fig. 2, in which curves II and IV are the low-pressure parts of the same isotherms in Fig. 1, plotted on a magnified pressure scale. The value of V/V_m found by the extrapolation of curve II to low pressures agrees well with the value found, by the subtraction of curve III from curve II, to be the amount of carbon monoxide that could not be pumped off sample C3 at −183°. This would be a function of the pumping speed and of the diameter of the arms of the sample holder. For comparison, 85% and 90% of a physically-adsorbed monolayer of nitrogen were removed by pumping under identical conditions for 45 min. and 2·5 hr. respectively at −196°. It seems reasonable to conclude, from the results in Fig. 2 and from the dimensions of the apparatus, that pumping at −183° removed carbon monoxide until the gas pressure fell to 10^{-5}—$10^{-6} p/p_0$.

Appreciable adsorption of carbon monoxide occurred at higher temperatures, where physical adsorption would be very small. Curves I and II of Fig. 3 are adsorption isotherms of carbon monoxide on specimen B1 in the reduced state, curve I being determined at −78° and curve II at +23°. Adsorption of carbon monoxide at these temperatures on C3 was similar but slightly smaller.

The adsorption of carbon monoxide at temperatures above room temperature was small.

A specimen of C3, which had been reduced in carbon monoxide at 600°, pumped at 680° until clean, and then exposed to 6 cm. pressure of carbon monoxide, adsorbed <1% of V_m at 680° and about 8% of V_m at 275°; the adsorption fell on raising the temperature again and the gas contained no measurable quantity of carbon dioxide at the end of the experiment.

Adsorption of Carbon Monoxide on Oxidised Uranium Dioxide Surfaces.—Uranium dioxide preparations that had adsorbed oxygen were still capable of chemisorbing carbon monoxide at low temperatures by a process very similar to that described above but the amount chemisorbed was smaller. The specimen of B1 previously studied was exposed to oxygen at −183°, and the oxygen pumped off at −183° and briefly at room temperature. The carbon monoxide isotherm at −183° determined after this treatment is shown as curve V in Fig. 1; the adsorption is less than on a reduced surface (I). The sample was pumped at −183° for 1·5 hr. and the isotherm redetermined: curve VI of Fig. 1 was obtained. A greater proportion of the adsorbed gas was removed by pumping at −183° than in the case of the reduced specimen, and the volume that could not be removed by pumping at −183° fell from $0{\cdot}77V_m$ to $0{\cdot}40V_m$. Chemisorption also occurred on oxidised surfaces at higher temperatures; curves III and IV of Fig. 3 show the adsorption of carbon monoxide at −78° and +23·5° respectively on sample B1 after the adsorption of oxygen; the adsorption was about half that occurring on the reduced oxide under the same conditions. All the adsorbed carbon monoxide was removed by pumping at room temperature.

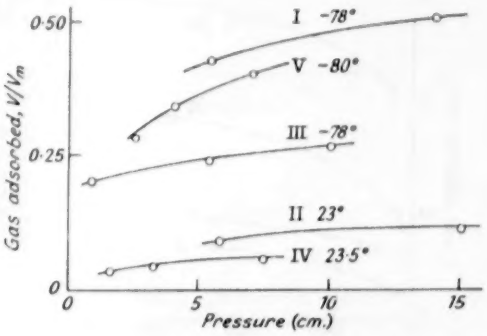

FIG. 3. *Adsorption of carbon monoxide on uranium dioxide and on thoria.*

Curves I and II—carbon monoxide adsorption on reduced uranium dioxide at −78° and 23°; III and IV—carbon monoxide adsorption on oxidised uranium dioxide at −78° and 23·5°; V—carbon monoxide adsorption on thoria at −80°.

The effect on the adsorption of carbon monoxide at −183° of progressively larger amounts of oxygen on the surface was studied in a series of experiments in which measured amounts of oxygen were allowed to be adsorbed on sample C3 and carbon monoxide isotherms determined after each addition. The volume of carbon monoxide that could not be pumped away at −183° (V_{CO}) was measured by repeating the −183° isotherm after pumping for 1—2 hr. at −183°.

TABLE 1.

Temp. of oxidation	Temp. at which O_2 removed	Total O_2 reacted (c.c., N.T.P.)	V_{CO} (c.c., N.T.P.)	Temp. of oxidation	Temp. at which O_2 removed	Total O_2 reacted (c.c., N.T.P.)	V_{CO} (c.c., N.T.P.)
—	—	0	0·470	—	—	0	0·268
−183°	−183° and 20°	0·136	0·328	−183	−183 and 20°	0·074	0·190
−183	−183 and −80	0·285 (V_0)	0·242	−183	−183 and 20	0·175 (V_0)	0·115
				20	20	0·665	0·062
—	—	0	1·15	120	20	2·11	0·062
−183	−183 and 20	0·76 (V_0)	0·60	120	110	3·49	0·083
				110	−80	4·19	0·068

The carbon monoxide was then finally removed by pumping for about 1 hr. at room temperature. The samples were also normally pumped at room temperature after the oxygen additions. Finally, one specimen was exposed to oxygen at higher temperatures, so that bulk oxidation occurred, and V_{CO} again measured. The results are collected in Table 1. Pumping times at the higher temperatures recorded in col. 2 were only a few minutes.

The maximum oxygen adsorption at −183° is denoted by the symbol V_0 in col. 3; oxygen adsorbed at higher temperatures in excess of V_0 is accommodated in interstitial positions in the lattice. The last results in Table 1 refer to B1; they are the results taken from Fig. 1.

The amounts of oxygen recorded in col. 3 have not been corrected for small losses due to reaction with carbon monoxide at room temperature.

It is evident from Table 1 that adsorption of quantities of oxygen less than $0{\cdot}5V_0$ caused V_{CO} to decrease by the same amount. Thus, in the first example, V_{CO} decreased by 0·142 c.c. when 0·136 c.c. of oxygen was adsorbed and, in the second, the adsorption of 0·074 c.c. of oxygen lowered V_{CO} by 0·078 c.c. Addition of more oxygen caused V_{CO} to decrease further, but by an amount quantitatively less than the amount of oxygen added. By the time V_0 of oxygen had been adsorbed, V_{CO} had been lowered by 68%, 87%, and 72% of V_0, in the three cases in Table 1. Bulk oxidation of the uranium dioxide lowered V_{CO} to about half the V_{CO} value characteristic of a surface on which V_0 of oxygen was adsorbed.

Oxygen Adsorption after Carbon Monoxide Adsorption.—A sample of B1 uranium dioxide that had adsorbed carbon monoxide at −183° and had been pumped at −183°—therefore retaining $V_{CO} = 0{\cdot}77V_m$, from Fig. 1—was exposed to oxygen at 183°; the isotherm measured is curve I in Fig. 4. The oxygen was pumped away for 30 min. at −183°, and the isotherm measured again—curve II in Fig. 4 is a plot of the results. The adsorption was very low compared with that of oxygen on a pumped, reduced surface (curve III) or with the physical adsorption of oxygen on the same surface after oxidation (curve IV). Curves I and II are not

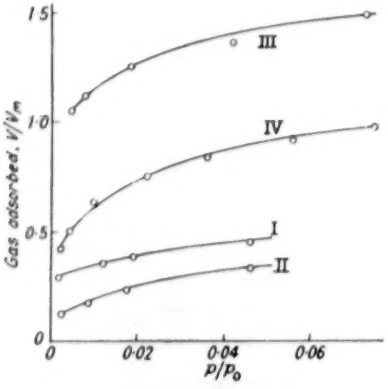

FIG. 4. *The effect of carbon monoxide adsorption on the adsorption of oxygen by uranium dioxide at* −183°.

Curves III and IV—adsorption of oxygen on reduced and oxidised uranium dioxide. Curve I—oxygen adsorption after chemisorption of carbon monoxide at −183°. Curve II—repeat of I after pumping at −183°.

strictly parallel, but they illustrate that all except $0{\cdot}1$—$0{\cdot}15V_m$ of the oxygen adsorbed on a surface saturated with carbon monoxide could be removed by pumping at −183°, whereas a clean surface chemisorbed $0{\cdot}51V_m$ of oxygen.

TABLE 2.

Sample	Total O_2 adsorbed or reacted (c.c., N.T.P.)	Conditions in CO: Temp.	Time	Pumping temp.	CO_2 found (c.c., N.T.P.)
R.61	0·136	20°	1·5 hr.	20°	0·0065
	$V_0 = 0{\cdot}285$	20	96 ,,	20	0·0157
	1·22	19·5	17 min.	19·5	0·0254
		,,	+17 ,,	,,	0·010
		,,	+20 ,,	,,	0·005
		,,	—	120	0·0256
R.60	0·074	20	30 ,,	20	0·00
	$V_0 = 0{\cdot}175$	20	16 hr.	20	0·00
	0·665	20	45 min.	20	0·025
	2·11	20	60 ,,	20	0·021
				120	<0·005
	3·49	20	16 hr.	20	0·047

Reaction of Carbon Monoxide with Adsorbed Oxygen.—During the experiments recorded in Table 1, the partially oxidised uranium dioxide samples were frequently allowed to remain in contact with carbon monoxide at room temperature for varying periods of time after the determination of the isotherms at −183°. The gas was gently circulated over the sample during this time and then analysed for carbon dioxide. The amount of reaction was very small; the results are given in Table 2. With only the oxygen adsorbed at −183° on the sample, carbon monoxide

removed in one experiment ~3% and in another <1% of the surface oxygen. After bulk oxidation had occurred, amounts of carbon dioxide corresponding to ~10% of the oxygen on the surface were found after long periods of exposure to carbon monoxide at 20°. At the end of the experiments on sample R.61 (Table 2), an equimolar mixture of carbon monoxide and oxygen was circulated at 8 cm. pressure over the sample for 24 min. at 20°; only 0·001 c.c. of carbon dioxide was found, but 0·014 c.c. of carbon dioxide was recovered by heating the sample to 120°.

Adsorption of Carbon Monoxide on Thoria.—A specimen of thoria was pumped at 750° and carbon monoxide isotherms were determined at −183°, again after pumping at −183°, and at −80°; V_m was determined by using oxygen at −183°. The two −183° isotherms were practically identical with the corresponding isotherms on B1 uranium dioxide, curves I and III of Fig. 1, and V_{CO}, the amount not removable by pumping at −183°, was $0{\cdot}78V_m$. The −80° isotherm is plotted as curve V in Fig. 3. It is evident that carbon monoxide is chemisorbed on thoria by a process very similar to its chemisorption on a reduced uranium dioxide. The thoria sample used chemisorbed only ~3% of V_m of oxygen at −183° after treatment with carbon monoxide at 700°.

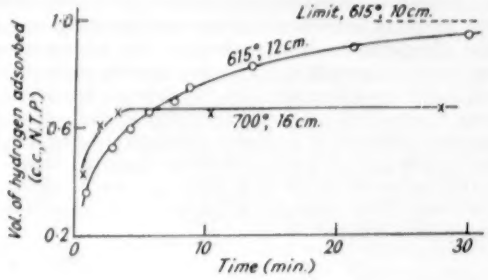

FIG. 5. *The rate of hydrogen adsorption on uranium dioxide at 615° and 700°.*

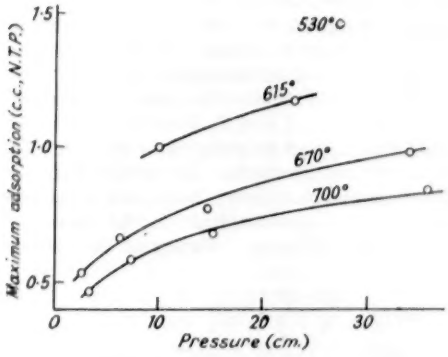

FIG. 6. *Hydrogen adsorption on uranium dioxide.*

Adsorption of Hydrogen by Uranium Dioxide.—A small adsorption of hydrogen occurred on reduced uranium at −183°:

Hydrogen pressure (cm.)	1·68	4·28	8·15
Hydrogen adsorbed (as V/V_m)	0·109	0·192	0·287

All the adsorbed hydrogen was recovered by warming to room temperature. No adsorption could be measured at 23° up to 25 cm. pressure.

Adsorption of hydrogen on reduced uranium dioxide proceeded at measurable rates above 470°. The quantity of hydrogen adsorbed on sample B1 at 615° and at 700° is plotted as a function of time in Fig. 5; the adsorbent had been reduced in hydrogen and pumped at 750° before these experiments. The adsorption apparently reached a final value in about 40 min. at 615° and in about 4 min. at 700°. The adsorption at 615° was shown to be pressure dependent. The rate of adsorption increased with increasing temperature: an approximate activation

energy of 35 kcal./mole was calculated by comparing the rates of adsorption at half the saturation adsorption at 615° and 700°. The hydrogen was slowly desorbed as such when the temperature was raised above 700°. The volume-calibration of the "Vitreosil" specimen bulb used was checked with helium at 700° and no loss of helium could be detected in 30 min.

The same specimen of B1 uranium dioxide was again out-gassed at 750°, and hydrogen adsorption followed to apparent saturation at various pressures at 700° and 670°. The maximum amounts adsorbed are plotted in Fig. 6: the 615° results are taken from the previous experiment. The single result at 530° was determined after 16 hr. at 530°. Approximate values for the heat of adsorption can be calculated if the system is assumed to be in equilibrium; values vary from 30 to 40 kcal./mole. Further adsorption occurred upon cooling to 475° and 415°. The final amount adsorbed was 1·94 c.c., or $1{\cdot}3V_m$, where V_m was measured as usual with oxygen at −183°.

In other experiments, the amounts of hydrogen adsorbed at low temperatures increased after exposure to hydrogen at high temperatures and repeated temperature cycling caused the total adsorption to increase slowly. The adsorption on one specimen of sample R increased from 0·24 c.c. to 0·55 c.c. after five heating cycles between 500° and 750°, the specimen being held at the lower temperatures for about 16 hr. and at the higher temperatures for 0·5—1·5 hr. Some water—0·05 c.c.—was recovered at the end of the experiment, leaving 0·50 c.c. as the maximum amount of hydrogen adsorbed; during the hydrogen treatment, V_m decreased from 0·46 to 0·30 c.c. A similar effect was observed on one specimen of sample C3. The adsorption at 460° increased from 0·55 to 0·85 c.c. after 3 heating cycles between 460° and 760°; no water was found in the hydrogen at the end of the experiment and V_m (nitrogen value) had decreased from 0·93 to 0·84 c.c.

Discussion

The adsorption of nitrogen on reduced or oxidised surfaces of uranium dioxide at −196° is very similar to that of oxygen on an oxidised surface at −183°, and such adsorption is therefore physical adsorption. The boiling point and molecular size of carbon monoxide are close to those of oxygen and nitrogen, and the physical adsorption of carbon monoxide at −183° should be similar to that of oxygen at −183° at the same relative pressure. The carbon monoxide isotherms actually measured (Figs. 1 and 2) therefore indicate chemisorption. The amount of carbon monoxide that cannot be pumped away at −183° (V_{CO}) will be taken as the amount chemisorbed at that temperature. The much smaller adsorption at −80° and at −23° shows that the heat of adsorption falls rapidly with increasing surface coverage. Approximate values of the heats of desorption may be calculated from the following equation (see Glasstone, Laidler, and Eyring, "Theory of Rate Processes," McGraw Hill Co., New York, 1941, p. 353):

$$\text{Rate of desorption} = C\,\frac{\boldsymbol{k}T}{\boldsymbol{h}}\cdot\frac{f^{\ddagger}}{f}\,e^{-E/\boldsymbol{R}T}$$

where C is the surface coverage and $f = f^{\ddagger}$. Times of half desorption of 10 min. are obtained with $E = 6$ kcal./mole at −183° and with $E = 21$ kcal./mole at 20°. Since the pumping speeds in the apparatus used would be low at low pressures, it is probable that V_{CO} comprises gas adsorbed with desorption energies of from 20 to 4 kcal./mole. It is unlikely that any of this gas is adsorbed in a second layer, but it is not certain that V_{CO} can be equated to complete surface coverage, since the heat of adsorption may fall to ~4 kcal./mole before all sites are occupied. A similar low-energy chemisorption of carbon monoxide on thoria was observed.

The depression of the adsorption of carbon monoxide on uranium dioxide by prior adsorption of oxygen, and of oxygen adsorption by prior adsorption of carbon monoxide, may be some evidence that both are adsorbed on the same sites, and it is very probable that adsorption of oxygen takes place on uranium sites. Studies of the adsorption of oxygen on mixed crystals of uranium and thorium dioxides (Part V, *loc. cit.*) confirmed that oxygen adsorption occurred only on uranium sites, where electrons could be donated to the oxygen. The type of carbon monoxide chemisorption studied here can take place on thoria and therefore does not depend on electron-donation to the adsorbed gas. A similar reversible, low-temperature chemisorption of carbon monoxide has been reported on zinc oxide (Garner, *J.*, 1947, 1239), on cuprous oxide (Garner, Stone, and Tiley, *Proc.*

Roy. Soc., 1952, *A*, **211**, 472), and on nickel oxide (Dell and Stone, *Trans. Faraday Soc.*, 1954, **50**, 501). The heat of adsorption is 26 kcal./mole on nickel oxide and 20 kcal./mole on zinc oxide; the heat of adsorption on cuprous oxide is 21 kcal./mole at 10% coverage, falling rapidly with increasing coverage. Adsorption on cuprous oxide is accompanied by electron donation from the gas to the substrate (Garner, Gray, and Stone, *Proc. Roy. Soc.*, 1949, *A*, **197**, 294) and the adsorption is held to occur on metal sites; 60% of the available metal sites are occupied at low pressures at −183° (Garner, Stone, and Tiley, *loc. cit.*). The marked lowering of the physical adsorption, as well as the chemisorption of oxygen on uranium dioxide by the previous adsorption of a chemisorbed layer of carbon monoxide at −183° (Fig. 4) is reminiscent of the depression of the adsorption of krypton on cuprous oxide by a partial layer of carbon monoxide, chemisorbed by a low-temperature process (Stone and Tiley, *Nature*, 1951, **167**, 654); carbon monoxide adsorbed in this fashion presumably alters the polarising properties of the surface, and subsequent physical adsorption of any gas resembles "second-layer" rather than "first-layer" adsorption.

Hydrogen is not much adsorbed at −183° and what little adsorption there is may well be physical adsorption, since the adsorption falls to zero at room temperature. The high-energy, activated process by which hydrogen is adsorbed above 400° resembles the processes of hydrogen adsorption by many oxides and oxide catalysts (Garner, *loc. cit.*; Taylor and Shou Chu Liang, *J. Amer. Chem. Soc.*, 1947, **69**, 1306), though the adsorption on the well-crystallised samples studied here took place at higher temperatures than on the "active" surfaces of catalysts prepared at low temperatures. Hydrogen adsorption had only a small effect on the subsequent adsorption of oxygen (Part V) and other work shows that the effect of hydrogen on low-temperature oxidation processes is also small. These results are compatible with hydrogen adsorption taking place on oxygen sites. The relatively small adsorption of carbon monoxide on uranium dioxide at 200° may also take place on oxygen sites, with the formation of a carbonate complex, as occurs on other oxides (Garner, *loc. cit.*). The carbon monoxide and hydrogen are desorbed at high temperatures as such, not as carbon dioxide and water, because of the thermodynamic stability of uranium dioxide.

The maximum amounts of oxygen, carbon monoxide, and hydrogen adsorbed on the uranium dioxide samples used were 0·5—0·6V_m, 0·7—0·8V_m, and 1·0—1·6V_m, respectively; V_m was always measured by physical adsorption of oxygen at −183°. These quantities represent very high surface coverages. On the assumptions that a physically adsorbed oxygen molecule occupies an area of 16·7 Å^2, equal to the usual nitrogen area, and that the planes having the highest density of U^{4+} ions—the (100) planes—are outermost, the number of U sites is 1·12 per physically-adsorbed oxygen molecule; this figure is reduced to 0·80 if the outermost planes are (110) planes. The minimum values for the surface coverage achieved by oxygen and by carbon monoxide at −183° are therefore 48% and 67% respectively if both are adsorbed as molecules. There are two O sites for each U site and an adsorption of 1·3V_m of hydrogen amounts to at least 60% surface coverage if one molecule is adsorbed on each O site or to at least 120% if the adsorption is dissociative. Since dissociative adsorption seems probable in the case of hydrogen, these results may point to some penetration of hydrogen into the lattice, which may explain the slowly rising figures for total adsorption found in some experiments involving repeated temperature cycling; solution of hydrogen in the lattice of tungsten sulphide has been postulated by Friz (*Z. Elektrochem.*, 1950, **54**, 538).

The quantitative agreement between the lowering of the carbon monoxide adsorption and the initial amounts of oxygen adsorbed (Table 1) could be explained if carbon monoxide and oxygen are both adsorbed as molecules on the same sites. That the carbon monoxide adsorption is not lowered to the same extent by subsequent increments of oxygen up to the V_O limit is probably explicable by some of the last increments of oxygen, which are adsorbed with a lower heat of adsorption (J. D. M. McConnell, personal communication), being lost from the surface sites during the brief period of pumping at room temperature before carbon monoxide was admitted. It is known that additional chemisorption of oxygen can occur after treatment at room temperature and that oxygen can dissolve in the uranium dioxide lattice at room temperature. The results in Table 1 then suggest

that 13—32% of the oxygen adsorbed at −183° is lost from the surface upon warming to 29°, on the assumption that the total number of sites available for oxygen and carbon monoxide adsorption remains constant. The further lowering of V_{CO} after bulk oxidation may mean that previously unoccupied sites are covered by oxygen after exposure to oxygen at 20° and above, or it may be a consequence of a change in surface energy levels due to interstitial positions in the lattice being filled with dissolved oxygen.

Some of the oxygen on the surface of uranium dioxide after bulk oxidation has occurred reacts slowly with carbon monoxide at 20° (Table 2). A reaction between carbon monoxide and adsorbed oxygen, with the extensive formation of carbonate complexes, has been found with other oxides (Garner, Stone, and Tiley, *loc. cit.*; Dell and Stone, *loc. cit.*). In the case of uranium dioxide, it is likely that only a fraction of the oxygen on the surface engages in such reactions, since the adsorption of carbon monoxide at 23° on a surface holding one layer of adsorbed oxygen was very small (curve IV, Fig. 3).

The author is indebted to Prof. J. S. Anderson for helpful discussion and criticism.

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The Oxides of Uranium. Part VII. The Oxidation of Uranium Dioxide.*

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Uranium dioxide is oxidised by two distinct processes in the temperature ranges −130° to 50° and 130° to 180°, though in each case oxygen is absorbed into interstitial positions in the lattice. Between −130° and 50°, the oxygen absorbed increases as the logarithm of the time; the same law is followed at the same temperatures by solid solutions of uranium dioxide and thoria. The oxidation virtually ceases at temperatures below 50° at a composition which depends upon the surface area of the uranium dioxide. Between 130° and 180° the kinetic law followed is characteristic of a diffusion-controlled process but both the rate of reaction and, to some degree, the composition of the oxide finally formed depend upon the pressure. The reaction with nitrogen dioxide is much faster than the reaction with oxygen.

The final products of the oxidation of uranium dioxide at moderate temperatures contain oxygen in interstitial positions in the original lattice and the course of the oxidation is not complicated by any abrupt phase change. Three processes of oxidation can be distinguished, taking place at different temperatures. The first proceeds rapidly at −183°, is probably confined to the surface, and consists of the adsorption of an oxygen molecule on at least 60% of the uranium atoms in the surface layer (Part V, *J.*, 1954, 3332). The second process can be followed at all temperatures from −130° to 50° on uranium dioxide itself and on those preparations of uranium dioxide–thorium dioxide mixed crystals which react with oxygen at −183°. Some results at 0° and 23° have already been recorded in Part V. More extensive results are presented below; it is shown that the extent of oxidation increases as the logarithm of the time of exposure to oxygen, and the effects of pressure and temperature are recorded. The third process occurs at measurable rates between 80° and 180°; this was first studied by Alberman and Anderson (*J.*, 1949, S 303). They showed that the kinetics of oxidation in air at several temperatures could be satisfactorily accounted for by a simple diffusion law with an activation energy of 27 kcal./mole. They reported, however, that the reaction rate was not independent of the oxygen pressure at low pressures. The last section of the present work is concerned with the dependence both of the rate of oxidation and of the final composition reached on the ambient oxygen pressure at a number of temperatures. The reaction of nitrogen dioxide with uranium dioxide at similar temperatures was also studied, since this is equivalent to using atomic

* Part VI, preceding paper.

oxygen (Katz and Gruen, *J. Amer. Chem. Soc.*, 1949, **71**, 2106) and should illustrate the influence of surface reactions on the bulk oxidation.

Experimental

Apparatus.—The low-temperature oxidation process, in which the amounts of oxygen reacting were small, was followed in the constant-volume, variable-pressure apparatus used for chemisorption studies (Part V, *loc. cit.*). The amount of gas reacting was determined by measuring the rate of fall of pressure on a mercury manometer; the total pressure variation was not allowed to exceed 15% of the original pressure. Since the rate of reaction changed only slowly with pressure, such pressure variations had little influence on the rates observed. The uranium dioxide was contained in a silica bulb or U-tube, which could be immersed in suitable freezing mixtures. Temperatures below 0° were measured with a pentane thermometer.

Different techniques were used for following the high-temperature oxidation process at high and at low pressures. At pressures from 2 to 500 mm., the amount of gas reacting was measured in a constant-pressure, variable-volume apparatus. The pressure was maintained constant automatically to $\pm$0·2 mm. at the lower pressures, and to $\pm$2 mm. at the higher pressures, by arranging that the flow of mercury into the gas burettes was controlled by a valve activated by an electrical contact fused in a mercury manometer in the reaction system. Pressures below 10 mm. were actually measured on a manometer filled with Apiezon "A" oil. The uranium dioxide was weighed into a silica U-tube which was fused inside a wide silica tube in which liquids of suitable b. p. were refluxed, thus maintaining a constant temperature during the reaction period. Accurate measurements could be made with this apparatus, but the volume of gas to be handled became inconveniently large at pressures lower than 2 mm.

At lower pressures, the kinetics were followed by measuring the gain in weight of a 0·3 g. sample of uranium dioxide suspended in a silica bucket weighing 0·2 g. from a silica spring having an extension of 1 mm. per mg. Measurements of the extension of the spring were made with a travelling microscope to $\pm$0·02 mm. The accuracy obtainable by this method was not as high as the gas-volumetric measurements allowed, but it was sufficient to enable the main features of the kinetics to be determined, since the total weight gain in any experiment was ~4 mg. The silica bucket hung in the middle of a double-walled silica jacket, in the annular space of which liquids were refluxed during the kinetic experiments, and which could be surrounded by a furnace for high-temperature reduction and outgassing. During a kinetic experiment, oxygen from a cylinder streamed continuously past the sample, the pressure being controlled by a needle-valve on the inlet side and by a stopcock between the specimen and the pumps; the oxygen stream passed through a liquid-oxygen trap immediately before entering the reaction tube. The pressure was measured by a Pirani gauge which had been calibrated against a McLeod gauge. The outlet to the gauge was situated about 4 in. from the sample, on the downstream side, the connecting tube being of 2 cm. internal diameter. Measurements made with another gauge the same distance from the first showed that the pressure drop in this length of tubing under the conditions used was negligible; the gauge thus measured correctly the pressure of oxygen surrounding the sample under flow conditions.

The preparation of the gases used for reduction and gas-volumetric measurements has been described in Part V (*loc. cit.*). The oxygen used was either B.O.C. "Spectroscopically Pure" oxygen or was prepared by heating A.R. potassium permanganate and passing the gas through glass-wool, potassium hydroxide, and a liquid-oxygen trap. A nitrogen dioxide–oxygen mixture was generated by heating dry lead nitrate crystals to 400—450°, after first outgassing them at 150°.

Uranium Dioxide Preparations.—Full details of the preparation and characterisation of the uranium dioxide specimens used have been given in Part V (*loc. cit.*). For convenience, the mean particle diameters, $\bar{d}$, as determined by gas-adsorption methods, are repeated here:

Specimen	B1	C3	H	R	CA	B50
$\bar{d}$ (in μ)	0·45	0·41	1·0	2·3	2·3	0·053

Results

Section 1. *Low-temperature Oxidation.*

General Procedure.—Each sample had to be reduced to stoicheiometric uranium dioxide before each oxidation experiment. Reduction was carried out either with hydrogen or with carbon monoxide at temperatures between 500° and 750°, and the sample was subsequently

outgassed at temperatures 50° above the reduction temperature. A partially fresh surface might be exposed each time by this treatment, because of the tendency of uranium dioxide containing excess of oxygen to form ordered phases at temperatures below 500° (Anderson and Alberman, *loc. cit.*). Ideally, therefore, the surface area should have been measured after each reduction. This was often done, but it was found that a series of reductions carried out on the same sample after successive slight oxidations caused only small changes in surface area, and, in what follows, the surface area is assumed not to change during such series of experiments. The errors introduced by this assumption should be small; for example, one sample decreased in area by 6% after seven cycles involving oxidation at temperatures below 30° and reduction at 500°, and four such cycles reduced the surface area of another sample by 10%.

The reaction of the reduced uranium dioxide with oxygen at the desired temperature and pressure was studied either at once or after exposure to oxygen at −183°, and pumping off the gas not adsorbed at −183° and at −78°. The total reaction at higher temperatures can be

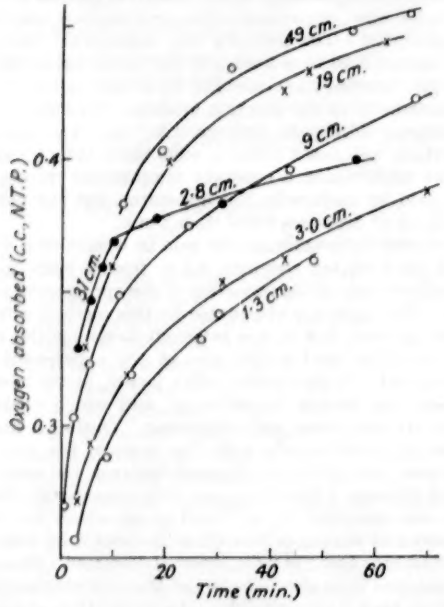


FIG. 1. *Oxidation of uranium dioxide at 19° and at various pressures.*

regarded as the sum of two quantities, a constant amount of oxygen chemisorbed even at −183°, and an amount characteristic of the higher temperature, the pressure of oxygen, and the time of reaction (see Fig. 3 of Part V of this series).

Oxygen could be admitted directly to samples of uranium dioxide at temperatures up to 50° if the particle size was 0·4 μ or larger. Specimens having mean particle diameters of 0·05 μ reacted pyrophorically if exposed directly to oxygen at 0°, but oxidised normally if exposed first at −80°, presumably because the heat evolved due to the rapid reaction at 0° on a reduced surface of large area could not be conducted away sufficiently rapidly. Specimens of particle size 0·4 μ reacted pyrophorically if exposed in the reduced state to oxygen at 150°.

No differences in reaction rates were found between specimens reduced in hydrogen and those reduced in carbon monoxide. Hydrogen is adsorbed on uranium dioxide at high temperatures, while carbon monoxide is not (Part VI, *loc. cit.*). A direct comparison was made between the absorption of oxygen at 0° and 10—12 cm. pressure on one sample of specimen C3, no. 50, which had been reduced with carbon monoxide and another, no. 65, which had been heated in hydrogen and had adsorbed 0·3 c.c. of hydrogen/g. After correction for a small difference in surface area, the results were as follows :

Time of reaction (min.)	0·55	1·85	32
Oxygen absorbed, sample 50 (c.c./g.)	0·37	0·40	0·50
Oxygen absorbed, sample 65 (c.c./g.)	0·32	0·335	0·42

Chemisorption of a considerable quantity of hydrogen thus caused a rather small decrease in the amount of oxygen absorbed at 0°. The effect on the reaction with oxygen of the small amounts of hydrogen that might have been left on the surface after reduction with hydrogen and high-temperature outgassing would therefore not be serious.

The Logarithmic Law.—Results obtained with specimen R at 19° and at pressures from 1·3 to 49 cm. are plotted in Fig. 1. The amount of oxygen reacting in a given time increased with increasing pressure, though the effect was rather small. However, suddenly dropping the pressure from 31 cm. to 2·8 cm. in one run, after the reaction had been proceeding for 10 min., caused a notable decrease in the rate of reaction, and raising the pressure from 3·0 to 13 cm. in another run after 70 min. caused some acceleration. The effect of pressure was thus not only an initial effect. The amount of oxygen absorbed in each case increased as the logarithm of the time of exposure, as is shown in Fig. 2, where the results of Fig. 1 are replotted against the logarithm of the time.

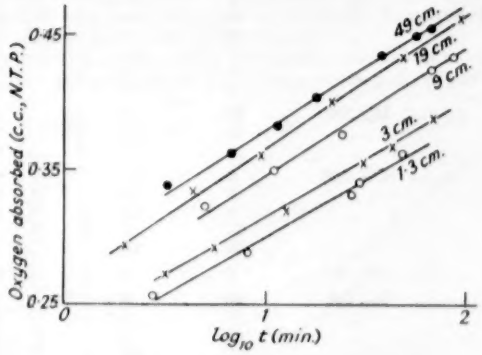


FIG. 2. *Logarithmic plot for oxidation of uranium dioxide at* 19°.

A logarithmic kinetic law was followed over the whole range in which the low-temperature process could be studied. If the fundamental equation is written

$$dc/dt = Ke^{-pc} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where c is the amount of oxygen absorbed in time t, and K and p are constants, then, if $c = 0$ at $t = 0$

$$c = (1/p) \ln (Kpt + 1)$$

If $Kpt \gg 1$, $c = (2{\cdot}3/p)(\log_{10} Kp + \log_{10} t)$, and the constants p and K can be evaluated from a plot of c against $\log t$.

In order to facilitate the comparison of results on different specimens, the quantity $(V - V_0)/V_m$ was plotted against $\log_{10} t$; V is the total quantity of oxygen reacting in t min., V_0 the amount of oxygen chemisorbed at −183°, and V_m the amount of oxygen required to form a single, physically-adsorbed monolayer on the specimen studied at −183°, as determined by application of the B.E.T. equation. The methods used in the evaluation of V_0 and V_m are discussed fully in Part V (*loc. cit.*). Essentially, $(V - V_0)/V_m$ represents the amount of oxygen absorbed by the time-dependent process studied here on a constant area of each specimen of uranium dioxide. The values of the constants K and p of the logarithmic law which were found in this way are recorded in Table 1, together with the values of $(V - V_0)/V_m$ reached in 30 min., which illustrate the magnitude of the amounts of oxygen reacting.

The results were reasonably reproducible as between the various specimens; the one general trend noted was that the rates of reaction of oxygen with specimen R were usually lower than with other specimens. It had previously been found (Part V, *loc. cit.*) that the chemisorption of oxygen per unit surface of specimen R was also lower than normal. The logarithmic law was found to hold for amounts of gas reacting of from $0{\cdot}05V_m$ to about $2V_m$ and for times of reaction ranging from 100 to 1000 min. The constant p of equation (1) decreased regularly as the temperature increased. The results on specimen R at 19° showed that the value of p was not much, if at all, dependent on pressure—as is illustrated by the straight-line plots in Fig. 2 being nearly parallel. The pressure dependence was due to the rise in the value of K as the pressure was increased. The values of K at a given pressure certainly decreased as the

temperature was lowered, although the K values were in general more variable than the p values. This is probably due to log Kp being estimated from the absolute amount of oxygen absorbed in a given time, once p had been determined from the slope of a logarithmic plot, and the value of K therefore depends on the conditions during the first moments when oxygen was admitted to the samples: results might be vitiated by local rises in temperature due to too rapid admission of gas or by lack of thermal equilibrium. Some such effect probably explains the extremely high K value found with specimen H at −113°.

TABLE 1. *Low-temperature oxidation of uranium dioxide.*

$(V - V_0)/V_m = (2{\cdot}3/p) \log Kp + (2{\cdot}3/p) \log t$ (min.).

Specimen	Reduction conditions	Oxidation at: Temp.	Pressure (cm.)	$(V - V_0)/V_m$ at 30 min.	p	$\log_{10} Kp$	K
H	H_2, 500°	−138°	(1·2)	0·065 *	59	0·17	0·025
	,,	−113	(2·3)	0·21 *	43	2·50	7·3
	,,	− 79	3·2	0·23	28	1·27	0·67
	,,	− 66	4·5	0·29	19·2	0·95	0·46
	,,	− 42	10·5	0·46	18·2	1·34	1·2
	,,	− 19	9·7	0·54	14·5	1·88	5·2
	,,	0	11	0·62	13·7	2·14	10·1
B1	H_2, 580	− 66	5	0·29	23·3	1·35	0·96
	,,	− 19	10	0·54	14·2	1·84	4·9
	,,	0	5	0·75	10·1	1·83	6·7
C3	CO, 580	0	17	0·45	13·1	1·72	4·0
	,,	0	13	0·71	10·1	1·65	4·4
	,,	0	12	0·50	13·4	2·31	15·2
	,,	25	5	—	9·2	—	—
	,,	51	12	1·40	5·6	1·84	12·4
CA	CO, 700	0	6	0·56	11·7	1·37	2·0
R	H_2, 530	− 66	6·5	0·19	35·7	1·55	1·0
	,,	− 21	7·5	0·33	20·6	1·49	1·5
	,,	0	7	0·49	13·9	1·42	1·9
	,,	19	49	0·66	9·3	1·53	3·7
	,,	19	19	0·64	8·6	1·20	1·8
	,,	19	9	0·56	9·9	1·00	1·01
	,,	19	3	0·50	10·3	1·00	0·97
	,,	18·5	1·3	0·47	10·2	0·85	0·69
B50	CO, 480	− 78	16	—	(98) (33)	—	—

* Corrected for physical adsorption.

The results found with specimen B50, which had a very large specific surface, were anomalous. Oxygen was admitted at −78° after first saturating the surface with oxygen at −183° and pumping the oxygen away at −183°, −78°, and 20°. An initial large absorption was followed by a very slow reaction ($p = 98$) for about 30 min., after which time the reaction rate increased and the p value found (33) was much the same as was found when using the preparations of larger particle-size at the same temperature.

Oxidation of UO_2–ThO_2 *Solid Solutions.*—The oxidation of these solid solutions at low temperatures also followed a logarithmic law. The constants K and p are recorded in Table 2.

TABLE 2. *Low-temperature oxidation of* $U_xTh_{1-x}O_2$ *preparations.*

Equation: $(V - V_0)/V_m = (2{\cdot}3/p) \log_{10} Kp + (2{\cdot}3/p) \log_{10} t$ (min.).

x	Oxidation conditions: Temp.	Pressure (cm.)	$(V - V_0)/V_m$ at $t = 30$	$(V - V_0)/V_0$ at $t = 30$	p	$\log_{10} Kp$	K
0·90	0°	10	0·57	1·26	15·7	2·20	10·0
0·82	0	7	0·53	1·27	15·8	2·17	9·3
0·82	23	8	0·73	2·15	9·3	1·50	3·4
0·66	0	6	0·37	1·20	15·3	0·97	0·60
0·66 C.C.	0	9	0·33	0·97	20·1	1·40	1·2
0·50 C.C.	0	7	0·26	0·96	22·8	2·00	4·4
0·24 C.C.	0	6	0·053	0·35	(90)	(0·57)	(0·04)
0·24 C.C.	23	6	0·14	0·95	38	0·88	0·20
0·15 C.C.	23	4	0·0075	0·068	115	0·46	0·025

In order to compare the amounts of oxygen reacting at 0° and at 25° with the amounts chemisorbed at −183°, values of $(V - V_0)/V_0$, as well as of $(V - V_0)/V_m$, at $t = 30$ min. are recorded in Table 2. Comparative values of $(V - V_0)/V_0$ for uranium dioxide can be read off from Table

1, since in this case $V_0 \sim 0{\cdot}5V_m$. The preparations denoted "C.C." had been prepared by crushing macrocrystalline sintered pellets of the solid solutions. All specimens were reduced with carbon monoxide at ~600° immediately before the oxidation measurements were begun.

The ratio $(V - V_0)/V_0$ decreased sharply when the mixed crystals were dilute in uranium—the amount of reaction in a given time at 0° or 23° decreased more rapidly than the amount of surface reaction. The p values found were roughly constant and comparable with those for uranium dioxide until the mole fraction of uranium dioxide in the solid solution became lower than 0·66, when p increased. The K values were again more variable, but in general decreased as the mole fraction of uranium dioxide decreased.

Vacuum Treatment after Partial Oxidation.—The oxygen absorbed at low temperatures was mobile above 100°. A sample of specimen C3 was oxidised for 30 min. at 0°, pumped at 170° for 2 hr., and oxygen again admitted at 0°, whereupon the oxidation followed the same course as initially on the reduced sample, the rate being about 0·9 of the initial rate. Again, a rapid absorption of oxygen occurred in the first 20 min. upon re-admission of oxygen to a sample (H) which had been pumped at 120° for 3 hr. after oxidation for 100 min. at 0°.

The same mobility did not occur at 25°. A sample of C3 was oxidised for 23 min. at 25° and then pumped at 25° for 3 hr. Oxygen was readmitted at the same pressure (~5 cm.) at 25° :

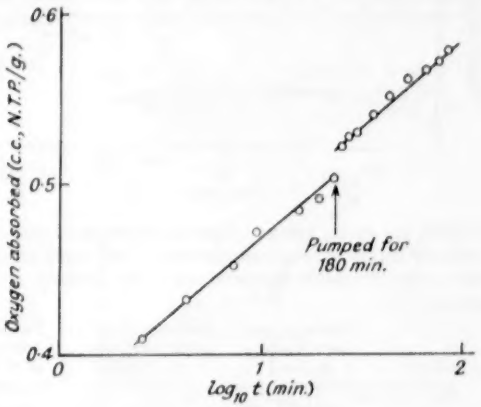


FIG. 3. *The effect of interrupting oxidation at 23° by pumping at 23°.*

a small adsorption, 0·02 c.c./g., occurred in the first minute, after which the oxidation continued as if there had been no interruption. The results are plotted in Fig. 3, in which the total oxygen absorbed is plotted against the total time of exposure to oxygen. The same result was obtained when oxidation at 23° was interrupted by the 16 hours' pumping at 23°. A similar, small effect was observed when oxidation at −113° was interrupted by 30 min. in vacuum at 20°.

These results indicate that the oxygen which has reacted does not leave the position it first occupied at 25°, but that it migrates away from the original position at temperatures above 100°, so that more can be absorbed into the same sites.

Limit of the Low-temperature Process.—The amounts of oxygen absorbed when a sample of C.3 was held in 12—20 cm. of oxygen and the temperature raised in stages from 0°—23°—51°—88°—124° are plotted in Fig. 4. Raising the temperature from 23° to 51°, after a long time of exposure to oxygen at 23°, caused only slight additional oxidation, but rapid acceleration of oxidation followed when the temperature was raised to 88° and to 124°. The oxidation above 88° was due to a different process, which was negligibly slow below 51°; this is the high-temperature process for which results are given in Section 2 (below).

It was clear from the results shown in Fig. 3, and from an extrapolation of the logarithmic plot of the oxidation of C.3 at 51°, that the low-temperature process could lead to the absorption of at least 1·0 c.c. of oxygen per g. of specimen C.3, or about $2{\cdot}5V_m$. Since $V_0 \sim 0{\cdot}5V_m$, the limit reached by $(V - V_0)$ is $\sim 2V_m$, or $4V_0$. A similar result was found on analysing small particle-size preparations, such as B.50, after exposure to air. These preparations were oxidised regularly and slowly if exposed to oxygen first at −183°, then at −78°, and then at slowly rising temperatures to room temperature. After finally standing in a desiccator at room temperature for 1—2 weeks, the composition was $UO_{2\cdot16}$—$UO_{2\cdot18}$: about 6·6 c.c. (N.T.P.) of oxygen had been

absorbed per g. Since, for these samples, $V_m \sim 2{\cdot}5$ c.c./g., oxygen had been adsorbed by the "logarithmic," low-temperature oxidation process to $\sim 2{\cdot}2V_m$, or $4V_O$.

Density Changes following Low-temperature Oxidation.—Work to be reported elsewhere has shown that the densities of uranium dioxide preparations oxidised at temperatures of 80—150° increase regularly and almost linearly with the amount of oxygen absorbed. These results refer essentially to high-temperature oxidation. Oxidation at low temperatures leads to composition changes too small to cause detectable density differences unless the particle size is very small. The methods of density measurement outlined in Part IV of this series (*J.*, 1954, 3324) were modified to allow for vacuum handling of highly reactive preparations, and the results

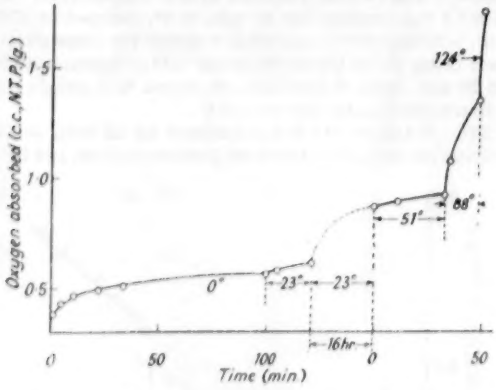


FIG. 4. *Continued oxidation of uranium dioxide at increasing temperatures.*

obtained are given below. The temperature of oxidation was always −78° at first and it was gradually raised to room temperature; too rapid oxidation led to the nucleation of a U_3O_8-like phase even at room temperature. The surface areas of the preparations used were ~11 sq.m./g.

Sample	Density, as as reduced (g./c.c.)	Density (g./c.c.) after oxidation at −183°	Density (g./c.c.) after oxidation at −78° and 20°	Final composition	Measuring fluid
B.50	10·82	—	10·66	$UO_{2\cdot 18}$	Toluene
	10·99		10·66		
B.55	10·79	10·47	10·53	$UO_{2\cdot 18}$	Toluene
L.16	10·99	10·35 *	10·78	$UO_{2\cdot 19}$	Helium

* This value may be low.

Before each density determination, the samples were outgassed at 20—50°. After oxidation at −183°, the oxygen was removed first at −183° and then at −78°, to prevent further oxidation occurring. The second sample, the density of which was determined with toluene, had to be heated to 100° under toluene to complete the outgassing; the third sample was never heated above 50°.

The density decreased upon oxidation at −183°; further oxidation at low temperatures caused an increase in density. The *X*-ray diffraction patterns of the final oxidised products were those of a slightly distorted UO_2-structure, with a contracted unit cell.

Section 2. High-temperature Oxidation.

General Procedure.—Specimens H and C.3 oxidised at convenient rates at temperatures of 130—180°, and were the only ones used in this study. Since the reaction of fully-reduced preparations with oxygen at these temperatures was pyrophoric, the high-temperature reaction had to be preceded by partial oxidation at low temperatures. Even then, a pyrophoric reaction would result if the reaction rate became too high. Thus, samples of specimen C.3 oxidised regularly at all pressures at 155° after 30 min. in oxygen at 30°, but the reaction was pyrophoric at high pressures at 165°, though the reaction was regular at low pressures at 165°. The particle size of specimen H was double that of C.3, and specimen H oxidised regularly at all pressures at 183° after 30 min. in oxygen at 30°.

It proved impossible to obtain reproducible results on samples from a bottle of specimen H

which had been exposed to air at room temperature for some years. Consequently, it was necessary to reduce each sample with carbon monoxide at 500—700°, and then to oxidise it under standard conditions at low temperatures before each high-temperature run: 30 min. in 12 cm. of oxygen at 30° were the usual conditions when using the gas-volumetric apparatus, and 30 min. in air at room temperature when using the silica-spring apparatus for low-pressure work. The samples were pumped out at room temperature and not pumped at the higher temperature for more than a few seconds before the high-temperature reaction was started. When using the gas-volumetric apparatus, oxygen at the required pressure was admitted as soon as the uranium dioxide sample attained the required temperature, the time of admission being taken as zero time; readings could be taken within 1 min. When using the silica-spring apparatus, the gas flow was adjusted to give the necessary pressure while the sample was at room temperature, and the sample was then heated, the time of reaching the required high temperature being taken as zero time; this procedure did not allow of such detailed study of the initial 10 min. of the reaction.

Reduction at high temperatures following bulk oxidation had more effect on the surface area than reduction following only low-temperature oxidation. Consequently, it was found more satisfactory to use a fresh uranium dioxide sample for each run than to use one sample with successive reductions. All the results quoted below were obtained by using one sample per run. However, a preliminary series of experiments made with one sample of specimen C.3

FIG. 5. *Oxidation of uranium dioxide* (H) *at various pressures at* 183°.

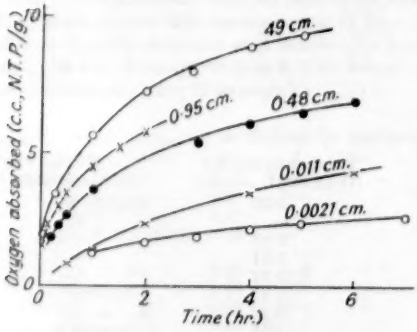
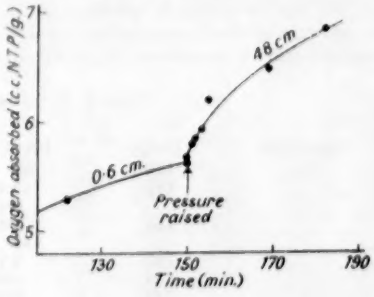


FIG. 6. *The effect of raising the pressure on the rate of oxidation of uranium dioxide at* 155°.



at various pressures from 3 to 48 cm. at 154° showed that the pressure had a definite effect on the rate of reaction. At the end of this series, the same sample was mixed with twice its weight of pure thoria, and the kinetic runs were repeated in exactly the same way at 12 and 48 cm. at 154°. The addition of the inert thoria made no difference to the rates of reaction. The particular geometry of the sample holder therefore had no effect on the course of the reaction.

The surface areas of the samples used were in many cases determined at the end of the oxidation by gas-adsorption methods, using nitrogen at −196° or krypton at −183° or at −196°. The surface areas of only 4 samples in 27 varied by more than 11% from average values characteristic of specimens C.3 and H; the kinetic constants given below were therefore not corrected for surface-area variations. Results reported elsewhere showed that no change of surface area occurred as oxidation proceeded.

Effect of Pressure on Oxidation Rate.—Some of the results obtained with specimen H at 183° and pressures of oxygen from 0·002 cm. to 49 cm. are shown in Fig. 5; these results illustrate the dependence of oxidation rate on pressure which was quite generally found on both specimens at all the temperatures studied; it can also be seen that the pressure had to be varied by some powers of 10 before the general trend was definitely established.

The rate of oxidation changed quickly when the pressure was altered. The result of raising the pressure to 48 cm. after one sample of C.3 had oxidised for 150 min. at 0·6 cm. is shown in Fig. 6: the rate of oxidation suddenly increased by a factor of about 8. A sample of specimen H was oxidised for 105 hr. at 183° and 0·48 cm., after which time the rate of oxidation had fallen to 0·01 c.c./g./hr. and the total absorption was 12·5 c.c./g. ($UO_{2\cdot30}$); the pressure was then raised to 24 cm. and a further 0·5 c.c./g. was absorbed in 5 hr. A sudden decrease in

pressure caused an abrupt drop in reaction rate. The oxidation rate of a sample of C.3 dropped by a factor of 5 when the pressure was lowered from 48 to 0·5 cm. after 52 minutes' reaction at 155°, and a similar change in pressure caused the oxidation rate of a sample of H to drop by a factor of 7 after 4·7 hours' reaction at 183°.

Many of the experiments were continued until the oxidation rate became zero—until no measurable absorption of oxygen occurred in 24 hr. The limiting compositions reached were to some extent a function of pressure. The compositions and a brief description of the *X*-ray characteristics of the final products are given in Table 3. The compositions quoted include the small amount of oxygen absorbed in the first low-temperature oxidation; the sign > means that oxidation had nearly but not quite stopped. The UO_2 structure is described as α; in the course of oxidation, the diffraction lines broadened in the sense of a contraction of the unit cell, until the β structure was reached: this is the cubic U_4O_9 phase. Oxidation much beyond the composition $UO_{2.25}$ led to tetragonal structures, eventually to the γ'' structure. The relationships between the α, β, and γ'' structures is discussed elsewhere by Anderson (to be published). In general, the structures of the final products of oxidation were those characteristic of the composition reached, irrespective of the temperature and of the rate of oxidation.

When the final composition was known, it was possible to fit the kinetic results to the simple equation for diffusion into spheres used by Alberman and Anderson (*loc. cit.*), *viz.*,

$$\frac{C}{C_\infty} = 1 - \frac{6}{\pi^2}\sum_1^\infty \frac{1}{n^2}\exp\left(-n^2 \cdot \frac{Dt}{a^2}\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where C is the oxygen absorbed at time t, C_∞ the maximum amount absorbed at $t = \infty$, a the radius of the particles, assumed to be spheres, and D the apparent diffusion constant. The equation can be tested by plotting C/C_∞ against $t/t_{\frac{1}{2}}$, where $t_{\frac{1}{2}}$ is the time when $C = 0{\cdot}5C_\infty$. The theoretical curve was closely followed by samples of C.3 at 154° up to $C = 0{\cdot}9C_\infty$, at all pressures, and by samples of H at 183° up to $C = 0{\cdot}6C_\infty$. Values of D were calculated from $t_{\frac{1}{2}}$,

TABLE 3. *Final products of oxidation.*

Specimen	Temp.	Press. (cm.)	Final composition (O atoms/U atoms)	*X*-Ray characteristics
H	184°	49	2·36	Tending to γ''
	182	45·7	—	—
		0·45	2·28	—
	183	0·48	2·31	—
		24	>2·32	—
	183	3·1	2·32	β, some γ''
	184	0·60	2·22	$\alpha - \beta$
	182	0·011	2·27	Distorted β
	182	0·0021	>2·21	α, contracting
	173	0·011	2·21	α + contracted α
C.3	154	48	2·38	γ''
	155	0·6	—	—
		48	>2·37	—
	155	3·2	2·36	γ''
	154	1·0	2·29	β, no γ
	154	1·0	2·26	β, poorly cryst.
	153	48	—	—
		0·5	2·24	—
	155	0·49	2·26	β, poorly cryst.
	154	0·0135	2·24	β, ?γ
	154	0·0020	2·27	β
	143	0·0135	2·24	—

since, from equation (2), $Dt/a^2 = 3{\cdot}02 \times 10^{-2}$ when $C = 0{\cdot}5C_\infty$. Values of D so found are listed in col. 6 of Table 4; a was assumed to be 0·5μ for specimen H, and 0·2μ for specimen C.3.

Not all the experiments could be followed to completion, because of the slow oxidation rates. It was found, however, that a parabolic law

$$C = K\sqrt{t} + A \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

was accurately followed at all temperatures and pressures up to a composition of $UO_{2.10}$. A plot of equation (3) for specimen C.3 at five pressures at 155° is shown in Fig. 7. Values of K and A are listed in cols. 4 and 5 of Table 4; C was measured in c.c. (N.T.P.)/g., and t in minutes. The values of the intercept A were rather variable, as might be expected since they depend

on the length of time of heating after the initial low-temperature oxidation before high-temperature measurements were started and, although conditions were standardised so far as possible, variations must have occurred.

The values of K showed, at all temperatures, a general dependence on pressure, and the apparent D values also decreased at low pressures. The general trend is well established by the results in Table 4, although exact values of the kinetic constants were difficult to determine,

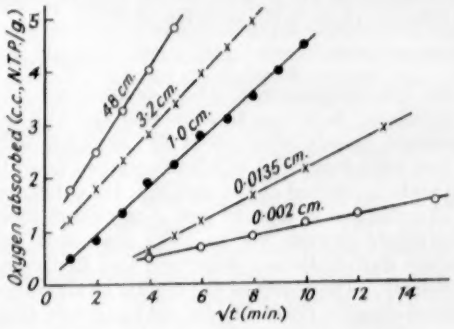


FIG. 7. *Parabolic plot of results for the oxidation of uranium dioxide* (C.3) *at various pressures at* 154—155°.

particularly at the lowest pressures reached. The times taken for specimens C.3 and H respectively to reach a given value of C/C_∞ under the same conditions were usually in the ratio 1 : 5, in good agreement with the prediction, from equation (2), that $t \propto 1/a^2$ when C/C_∞ is constant, which leads to a predicted ratio of 1 : 6.

TABLE 4.

Specimen	Temp.	Press. (cm.)	K	A	$10^{15}D$ (cm.²/sec.)	Specimen	Temp.	Press. (cm.)	K	A	$10^{15}D$ (cm.²/sec.)
C.3	164·5°	12	0·82	0·45	—	H	184°	48	0·65	0·7	—
	164·5	3·2	0·69	1·0	—		183	49	0·70	0·4	—
	164·5	1·0	0·57	0·9	—		184	49	0·73	0·4	8·9
	163·3	0·0135	0·25	0	—		182	46	0·59	0·4	—
							183	3·1	0·40	0·7	5·2
	154	48	0·80	0·9	2·50		183	0·95	0·47	0·8	—
	153·4	48	0·62	0·5	—		184	0·60	0·29	1·5	7·7
	155	3·2	0·53	0·8	1·52		183	0·48	0·40	0·4	4·8
	154	1·0	0·43	−0·2	0·83		183	0·20	0·37	0·75	—
	154	1·0	0·45	0	0·83		182	0·011	0·26	0	1·9
	155	0·6	0·40	0·2	—		182	0·0021	0·11	0·8	—
	155	0·49	0·39	0·8	1·67						
	154	0·0135	0·24	−0·2	0·37		173·4	0·0135	0·16	−0·2	1·2
	154	0·0023	0·10	0·1	—						
	154	0·0020	0·20	−0·3	0·15		165	48	0·41	0·2	—
							165	48	0·44	0·0	—
	143·4	0·0135	0·19	−0·1	0·22		165	49	0·45	0·15	—
							165	6·4	0·265	0·1	—
	131	48	0·35	0·4	—		165	1·0	0·26	0·35	—
	131	48	0·24	0·1	—		165	1·0	0·32	0·3	—
	131	12·2	0·25	0·25	—		163	0·30	0·22	1·1	—
	131	1·1	0·21	0·30	—		163	0·011	0·12	−0·25	—
							155	48	0·42	−0·3	—
							153	48	0·29	0·05	—
							154	0·97	0·22	0·35	—
							155	0·25	0·17	0·2	—
				Oxidation in ½ atm. of O_2–NO_2 mixture :							
C.3	155	—	1·44	0·8	—	C.3	131	—	0·64	0·8	—

Oxidation with Nitrogen Dioxide.—Oxidation for a long period of specimen C.3 at 131° and at 155° in an oxygen–nitrogen dioxide mixture gave a highly oxidised product containing structures other than fluorite. However, the initial periods of the reaction—until a composition $UO_{2.26}$ was reached, which took 5·5 hr. at 131° and 1·3 hr. at 155°—were apparently similar to the oxidation with oxygen at these temperatures, and the products showed a poorly crystalline

U_4O_9 *X*-ray diffraction pattern. Weight gain due to adsorption of nitrogen dioxide was corrected for by pumping at 155° at the end of each experiment and subtracting the weight decrease found from the overall weight gain: the adsorption was small at 155°. Adsorption of nitrogen dioxide was so extensive at 100° that the kinetics of oxidation could not be followed, a similar result to that obtained by Katz and Gruen (*loc. cit.*). The parabolic constants, K, determined from the corrected kinetic curves are recorded at the bottom of Table 4. The rate of oxidation was at least twice as large in $\frac{1}{2}$ atm. of a nitrogen dioxide–oxygen mixture as in $\frac{1}{2}$ atm. of oxygen at the same temperature.

Discussion

The low-temperature and high-temperature processes represent two quite distinct modes of oxidation; it is easy to show that the high-temperature process would not proceed at measurable speeds below about 70°, since the activation energy is too high. Either there are two mechanisms by which oxygen can enter the uranium dioxide lattice or a different final state is reached at low and high temperatures.

The changes in density and *X*-ray characteristics as oxidation proceeds by the high-temperature process (80° to 180°) show that oxygen enters interstitial positions in the uranium dioxide lattice (Alberman and Anderson, *loc. cit.*; Anderson and Roberts, to be published). The study of the similar oxidation of solid solutions of uranium dioxide and thorium dioxide (Part IV, *loc. cit.*) suggests that the factors which limit the amount of oxygen that can enter the uranium dioxide lattice in this way are essentially geometrical.

The *X*-ray and density evidence obtained on small-particle preparations which oxidised to a considerable extent by the low-temperature process suggest that the final products closely resemble oxides of the same composition obtained by high-temperature oxidation of large-particle specimens. The broad diffraction lines caused by the small crystallite size render exact comparison of the *X*-ray patterns difficult, but the unit cell does tend to contract as oxidation proceeds. The density also rises as low-temperature oxidation proceeds, although when oxygen is first admitted to a reduced uranium dioxide, the density falls. The results given above suggest that this fall in density is associated with the formation of the first chemisorbed layer of oxygen, complete at −183°. The adsorption of a layer of oxygen on the surface of uranium dioxide would be expected to cause a decrease in density; a quantitative calculation cannot be made accurately until the state in which the oxygen is adsorbed is known, as well as the distribution on the surface. Nevertheless, the density decrease may be approximately calculated if the chemisorbed layer is assumed to be equivalent to a layer of $O^{=}$ ions, of diameter 2·8 Å, covering the surface of each particle. The density of a uranium dioxide particle of 500 Å diameter would then fall by 3·3% owing to chemisorption; further inclusion of $\sim 0{\cdot}14O/UO_2$ interstitially would cause a density rise of 0·9%, and the overall result of oxidising a uranium dioxide preparation of this particle size to $UO_{2\cdot18}$, if all the extra oxygen except the surface oxygen entered interstitial positions, would be a fall in density of ~2·4%, a prediction which is close to the observed values. If the extra oxygen were accommodated by the creation of cation vacancies, the density would continue to fall as oxidation proceeded, and the density of $UO_{2\cdot18}$ would be about 10% below that of $UO_{2\cdot00}$.

Low-temperature oxidation would then appear to lead to the filling of interstitial positions by oxygen in much the same way as high-temperature oxidation. The interstitial positions filled seem to be those nearest the surface, since the limiting compositions reached before oxidation becomes extremely slow are dependent not on gross composition but on surface area, the limiting amount of oxygen entering the lattice being $\sim 2{\cdot}2V_m$. The high-temperature oxidation comes to an end when each unit cell accommodates 1—1·5 extra oxygen atoms. If each unit cell near the surface provides 1 interstitial position which can be filled by low-temperature oxidation, then the number of such positions in one layer is $0{\cdot}28V_m$, if the area of an oxygen molecule, used to measure V_m, is assumed to be 16·4 Å^2. Then the penetration below the surface of the oxygen that enters by the low-temperature process is $2{\cdot}2/0{\cdot}28 = 8$ unit cells, or 44 Å. Further, the regeneration of the absorptive capacity for oxygen at low temperatures by heating in vacuum to temperatures above 100° also indicates that low-temperature oxidation occurs only near the

surface, and that further oxidation can occur only when the oxygen that has entered the lattice receives enough energy to permit migration into the interior.

The formation of a thin film (~50 Å) of oxidised uranium dioxide near the surface, at temperatures too low for normal migration of oxygen through the lattice, is reminiscent of the formation of thin films of oxides on metals at temperatures too low for normal migration of metal ions through the oxide layer. This has been explained by Mott and Cabrera (*Reports Progr. Phys.*, **1949**, **12**, 163) as being due to the high electrostatic field set up between the metal and the adsorbed oxygen ions, which accelerates the outward motion of the positive metal ions through the oxide film if the film is thin. Some similar mechanism may be operative here, accelerating the inward motion of the negative oxygen ions. Mott and Cabrera showed that, in certain circumstances, this mechanism may lead to a logarithmic kinetic law. Consideration of the electrostatic field set up between the surface and the interior of a *p*-type semiconductor upon adsorption of an electron-accepting molecule, which increases the concentration of positive holes near the surface, has been shown by Engell and Hauffe (*Z. Elektrochem.*, **1953**, **57**, 762) to lead to a logarithmic relation of the form of equation (1), but where C is the amount chemisorbed at time t. Their treatment cannot be directly applied to our case, where the chemisorption is rapid and constant and the oxygen reacting by the logarithmic law penetrates into the solid. There is in any case the difficulty that any such explanation would seem to predict that, as long as the chemisorbed layer remains intact, some inward motion of the interstitial oxygen should continue as long as the oxidised film is very thin. This does not seem to be the case. Even though at least 70% of the chemisorbed layer is stable to evacuation at 20° (Part V, *loc. cit.*), the results of experiments in which the logarithmic oxidation at 20° was interrupted by long periods of pumping (at ~10^{-4} mm.) at 20° showed that the interstitial oxygen had not left its original positions; if inward migration had continued in the absence of oxygen in the gas phase, then an accelerated reaction would have occurred when oxygen was re-admitted.

The occurrence of low-temperature oxidation, by the same kinetic law, on all the uranium dioxide–thoria solid solutions which chemisorbed oxygen shows that the process is a general one characteristic of the lattice type and the interaction of uranium and oxygen. Adequate theoretical explanation must await data on the energetics of the various steps involved.

The High-temperature Process.—Perio (*Bull. Soc. chim. France*, **1953**, 256) has argued that the oxidation of uranium dioxide at temperatures below 175° proceeds by formation of a skin of a tetragonal oxide, of composition $UO_{2\cdot32}$. A recent study of the profiles of the *X*-ray lines of oxidised specimens of C.3 and H uranium dioxide (Anderson, to be published) shows, however, that they are compatible with a regular concentration gradient of interstitial oxygen being set up inside each particle, and that ordered structures, $UO_{2\cdot25}$, $UO_{2\cdot31}$, and $UO_{2\cdot375}$, are formed during the later stages of oxidation. The final composition reached was dependent on the pressure (Table 3), though it was not a smooth function of pressure. In a large number of the experiments at lower pressures, the final composition was close to U_4O_9 ($UO_{2\cdot25}$), and the *X*-ray pattern of the final product was that of a poorly-crystalline U_4O_9. The final composition reached before oxidation became extremely slow at these temperatures may have depended on the ratio between the rate of oxidation and the rate of ordering of the interstitial oxygen, which would be a function of concentration and temperature. When the oxidation rate was slow, at low pressures, the U_4O_9 structure might have had a chance to form and the oxidation therefore stopped at this composition; other experiments showed that well-annealed U_4O_9 oxidised extremely slowly below 200°. When the rate of oxidation was fast, oxygen may have occupied random interstitial positions more quickly than the ordering process to U_4O_9 could take place, and one of the ordered tetragonal phases was formed. At very low pressures, the oxidation ceased at a composition below $UO_{2\cdot25}$, and there was *X*-ray evidence that some unoxidised $UO_{2\cdot0}$ remained; this seems to indicate that, in these cases, the oxidation was so slow that the ordered structure could be formed as a surface skin, inhibiting further oxidation.

The form of the kinetic law followed, and the fact that interstitial oxygen could diffuse away from the surface in the absence of oxygen in the gas phase as soon as the temperature

was raised above 100°, suggest that the high-temperature process was essentially diffusion-controlled, which was the view put forward by Alberman and Anderson (*loc. cit.*). However, for a diffusion-controlled reaction, not only should equation (2) be followed in every case, but, at any temperature, the values of D, the diffusion constant, should be the same at all pressures. This was not so; the values found for D (Table 4) decreased at low pressures. This result may be explained in one of two ways: (i) The surface concentration of mobile oxygen quickly comes to a value characteristic of the pressure at any temperature, but which is not equal to C_∞, the limiting composition reached. In view of the discussion above of the ordering processes which probably determine the limiting composition, this is not unlikely. The D values are calculated from the time taken to reach $C = 0{\cdot}5C_\infty$, and if C_∞ is not equal to the surface concentration controlling the diffusion process, the variation of D values with pressure is explained. Alternatively, (ii) the surface process may not always be rapid compared to diffusion. The overall rate of reaction may be determined partly by the rate at which a vacant interstitial site near the surface is occupied by oxygen from the gas phase, and be diffusion-controlled only in the sense that oxygen has to migrate into the interior before vacant sites near the surface can be regenerated. The process is then equivalent to diffusion with a variable surface concentration. At low pressures, the rate would be determined mainly by the rate of the surface reaction, whereas at high pressures, the slow stage would be diffusion into the interior.

The evidence seems to favour a process of type (i). Interstitial sites near the surface are rapidly filled even at low temperatures, and values obtained for the activation energy at different pressures, although rather variable, showed no definite dependence on pressure, which may point to the same diffusion process being rate-controlling at all pressures.

The diffusion equation, equation (2), reduces at small values of C/C_∞ to the parabolic form

$$C/C_\infty = K_1\sqrt{D}\sqrt{t}$$

where K_1 is a numerical constant. Hence the constant K of equation (3) is proportional to $\sqrt{D}$, and the apparent activation energy of the diffusion process may be calculated from the variation of K^2 with temperature. The results obtained are given below; averaged values of K for a given temperature were used.

Pressure (cm.)	48	12	1	0·25	0·013
E, kcal./mole (spec. H)	18	—	20	21	24
E, kcal./mole (spec. C.3)	27	25	22	—	14—18

These values for the activation energy, E, may be compared with the value of 27 kcal./mole reported by Alberman and Anderson (*loc. cit.*) and with the value of 24 kcal./mole calculated from the K values for the reaction with nitrogen dioxide. The E values showed no definite trend with pressure, as has been reported by Moore and Lee (*Trans. Faraday Soc.*, 1951, **47**, 501) for E values calculated from parabolic constants for the oxidation of zinc, between 370° and 400°, which were also dependent on the pressure.

If the effective concentration of interstitial oxygen near the surface is indeed a function of pressure, then the large variation in K observed, more than a factor of 10 if the nitrogen dioxide experiments are included, would seem to require that C_∞ be lower than 0·25/U atom at low pressures, since the concentration of interstitial oxygen can never be greater than 1 O atom/U atom. This suggests that the continuation of the oxidation up to the C_∞ values observed at low pressures, which was a very slow process, may be due to the ordering tendency discussed above, which would lead to interstitial atoms tending to occupy positions in neighbouring unit cells, thus denuding some areas of interstitial oxygen and enabling oxidation to proceed. This view is not incompatible with the eventual formation of a "skin" of U_4O_9, which was proposed above to account for the diffraction patterns of the final products.

The kinetics of oxidation may therefore be controlled at different stages by different processes. Nevertheless, the experiments which involved rapid pressure changes while oxidation was proceeding showed that the oxidation, both at low and at high temperatures, was immediately sensitive to changes of pressure. It seems, therefore, that the concentration of oxygen which can potentially diffuse into the interior is reversibly pressure

dependent. At any temperature, the parabolic constant K was proportional to p^n, where n varied from 0·13 to 0·16 and was usually between 0·15 and 0·16. The surface concentration of oxygen which can migrate inwards therefore follows a Freundlich adsorption isotherm.

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The Polonium Halides. Part II. Bromides.*

By K. W. Bagnall, R. W. M. D'Eye, and J. H. Freeman.

[Reprint Order No. 6411.]

Polonium dibromide and tetrabromide and ammonium and cæsium hexabromopolonite have been prepared. A dichlorodibromide and a tetrabromide ammine have also been obtained. Some properties of these compounds have been investigated. The crystal structures of the tetrabromide, ammonium and cæsium hexabromopolonite, and cæsium hexabromotellurite have been determined.

Joy (*Chem. Eng. News*, **1954**, **32**, 3848) has reported the existence of polonium tetrabromide as a dark red solid (m. p. 324°, b. p. 360°/200 mm.) which was prepared (Burbage, American report MLM 885, 1953, 18) by heating the metal in bromine vapour at 200 mm. for one hour at 250°. The polonium content was determined calorimetrically, and the bromide content by potentiometric titration against silver nitrate. Burbage (*loc. cit.*) reports that attempts to prepare polonium dibromide were unsuccessful.

Experimental

The preparative and analytical techniques described in Part I * were used in this work.

Handling of High-level Sources.—Some of the difficulties experienced in handling high-level sources of high specific activity have been mentioned in previous papers (Bagnall and D'Eye, *J.*, 1954, 4295; Part I, *loc. cit.*) and it is desirable to repeat that the specific activity of ^{210}Po is 4·5 c/mg. and that 1 curie represents 5×10^7 tolerances of ingested ^{210}Po. It is therefore essential to keep curie quantities of the element under control in sealed systems. This is complicated, in the X-ray work, by the disruptive effect of the α-bombardment on the glass capillary, which after a few days begins to show a crazed appearance around the polonium, possibly owing to recrystallisation of the glass. The area in contact with the polonium therefore becomes very fragile, and after a week the capillaries tend to break around the contact area and, in some cases, to explode under the gas pressure within the tube. For an X-ray capillary 1 cm. long and of 0·2 mm. internal diameter (volume = 0·3 mm.^{3}) the helium generated per day per curie would occupy 0·12 mm.^{3} at S.T.P. and would therefore exert a pressure of approximately 0·4 atm. The halogen liberated in the change from quadrivalent polonium to bivalent lead would also generate an equivalent increase in pressure. It will therefore be seen that the total pressure inside the capillary could build up to about 6 atm. in a week for a 1-curie sample. With a 19-cm. Unicam Debye–Scherrer powder camera, exposure times in the range 24—36 hr. were used and increasing the amount used for each X-ray photograph increased both the rate of attack on the glass and the rate of increase of gas pressure within the capillary. The vigorous radiation decomposition of solvents under the intense α-bombardment has been described before (Bagnall and D'Eye, *loc. cit.*; Part I, *loc. cit.*) and this is also accompanied by erosion of the glass container.

Owing to the readiness with which the element and its compounds react with oxygen, and to the high vapour pressures of the halides, it has not been found practicable to handle this element or its compounds in open tubes.

On the last occasion when an X-ray capillary was broken on transfer to the camera, the laboratory could only be entered by persons wearing gas-masks or air-hoods and the floor covering had to be removed in its entirety owing to the widespread contamination.

In this work one curie (0·2 mg.) has been used for each experiment and all reported results

* Part I, *J.*, 1955, 2320.

are the product of duplicate (in the case of analyses quadruplicate) experiments. It should also be noted that lead grows into each preparation at the rate of 0·5% per day, so that each preparation must be recovered and purified by electrodeposition (Part I, *loc. cit.*) before it can be used again.

Results

Analytical.—The atomic ratio of bromine to polonium in the tetrabromide was found to be 4·1 ± 0·1, and in the dibromide 1·85 ± 0·05. The low results are believed to be due to adsorption of bromide ions on the precipitate formed by the decomposition of the dibromide by 0·1N-nitric acid for analysis. The bromine content of the cæsium hexabromopolonite preparations was always 5—10% high (Br/Po = 6·3—6·6), owing to occluded cæsium bromide in the precipitates, identified by *X*-ray powder photography. The dichlorodibromide analyses gave a total halogen content consistent with the formula $PoCl_2Br_2$, although the chloride end-point was not well defined. In view of the method of preparation the composition must be $PoCl_2Br_2$.

Polonium Tetrabromide.—The tetrabromide is a bright red solid, melting in bromine vapour (sealed tube) at about 330° (cf. Joy, *loc. cit.*, 324°) to a dark liquid. At 250° in air or oxygen it is converted into the dioxide.

It was prepared by dissolving polonium metal or dioxide in hydrobromic acid and slowly evaporating the resulting solution to dryness, by heating the metal in a stream of dry bromine vapour, diluted with nitrogen, at 200—250° for 5 min., and by heating the dioxide in dry hydrogen bromide. Polonium metal does not react readily with bromine (liquid or vapour) in the cold.

The tetrabromide dissolves in dilute hydrobromic acid to give an orange red (10^{-3}M) or carmine-red (0·025M) solution. Addition of aqueous cæsium bromide solution to a 10^{-3}M-solution of the tetrabromide in 2N-hydrobromic acid yields an immediate precipitate of dark red cæsium hexabromopolonite. This compound decomposes at 300° into cæsium bromide and polonium bromides and is immediately hydrolysed by cold water. Preparations for *X*-ray powder photography were washed with absolute alcohol. The corresponding potassium and rubidium salts are soluble in 2N-hydrobromic acid.

The tetrabromide is soluble in hydrobromic acid solution, in ethyl alcohol, acetone, and some other ketones. It is sparingly soluble in liquid bromine and is insoluble in benzene and carbon tetrachloride. It is hygroscopic and on hydrolysis yields a white solid of indefinite composition, presumably a basic bromide.

A blackish-brown precipitate was obtained by cooling a hydrobromic acid solution of the tetrabromide to −30°. This is possibly a complex acid of the form $PoBr_4,xHBr,yH_2O$ (cf. tellurium) and is unstable at room temperature, forming a solution of the tetrabromide in hydrobromic acid.

The tetrabromide is rapidly reduced in solution to the purple, bivalent state by sulphur dioxide or hydrazine in the cold. The reduced solutions are re-oxidised to the quadrivalent state in *ca.* 480 sec. as found for the tetrachloride (Part I, *loc. cit.*). Unlike the tetrachloride, the oxidation potential–time curve shows no evidence for the existence of an intermediate tervalent bromide.

Polonium Dibromide.—The dibromide is a purple-brown solid which sublimes with slight decomposition at 110°/30 microns). It melts in nitrogen, apparently with disproportionation, at 270—280° (sealed tube) and the products appear to recombine on cooling. It is prepared by thermal degradation of the tetrabromide at 200° under vacuum and by reduction of the tetrabromide by hydrogen sulphide gas in the cold. The identity of these compounds was confirmed by *X*-ray powder photography. Sulphur dioxide gas partially reduces the dry tetrabromide to dibromide.

It is soluble in a number of ketones and in dilute hydrobromic acid, giving purple solutions which are rapidly oxidised to the quadrivalent state. 0·1N-Nitric acid decomposes the dibromide with the formation of a white precipitate of unknown composition.

Interhalogen Compounds.—Polonium dichloride reacts readily with bromine vapour at room temperature to give a salmon-pink product which is probably $PoBr_2Cl_2$. *X*-Ray powder photography indicated the absence of dichloride, tetrachloride, and tetrabromide, but the photographs were too poor to give definite proof of a new compound. Even if the product is an equimolar mixture of tetrachloride and tetrabromide, it could only be formed by disproportionation of a dichlorodibromide, since, under the conditions of the experiment, the dichloride does not disproportionate to tetrachloride and metal, and the metal does not react with bromine.

Solid polonium dibromide does not react with iodine vapour.

Polonium–Bromine–Ammonia System.—The reactions of the tetrabromide with dry ammonia

are rather complex. At room temperature one series of preparations gave an unstable yellow addition compound which, when prepared in an *X*-ray capillary tube, blackened after 2 hr. and after 24 hr. was resolved into discrete bands of polonium metal, polonium tetrabromide, and ammonium bromide, indicative of the high internal temperature of the sample. However, when prepared for analysis in a tube of 6 mm. internal diameter, the decomposition products, after 24 hr., appeared to be polonium dibromide and ammonium bromide only. This difference is possibly due to the lower thermal capacity of the capillary and its consequent higher temperature. A second series of preparations for analytical purposes, however, resulted in the disappearance of the polonium tetrabromide in the ammonia stream, presumably in the form of a volatile, colourless ammine. No analytical data on the composition of these compounds could be obtained and the reason for this different behaviour could not be ascertained.

When polonium tetrabromide is heated in dry ammonia gas at atmospheric pressure and at 100°, the product is mainly brick-red ammonium hexabromopolonite, identified by *X*-ray powder photography, which sublimes, apparently unchanged, at 200°/1 atm. When this compound was heated in a sealed tube at 200° it blackened and detonated, shattering the container, suggesting the possible formation of polonium nitride, analogous to the explosive tellurium nitride, Te_3N_4 (Strecker and Ebert, *Ber.*, 1925, **58**, 2527).

No dibromide ammines were obtained, and polonium dibromide is immediately reduced to the metal when heated in ammonia gas.

Organic Compounds.—Polonium tetrachloride and tetrabromide appear to condense with mono- and di-ketones to form compounds which may be analogous to the corresponding tellurium derivatives (*e.g.*, see Morgan and Drew, *J.*, 1925, **127**, 531). Two series of crystalline compounds have been prepared, one containing halogen [chloride (yellow) or bromide (orange)] and one containing no halogen (purple-violet) obtained from the first series by heating or by shaking with potassium hydroxide solution, and by reaction of polonium dihalides with ketones. Work on the analysis of these compounds is continuing.

X-Ray Crystallography.—The crystallography of the polonium compounds has been complicated by the poor diffraction photographs (Bagnall and D'Eye, *loc. cit.*; Part I, *loc. cit.*). The lines were rather diffuse and faded away at a Bragg angle $\theta = 40°$. In our earlier work the poor photographs were attributed mainly to the small amount of sample used (0·2 mg.), a micro-focus tube not being available. More recently, the quantity of sample used has been increased but with no substantial improvement in the diffraction photographs. The background on the photograph is necessarily high owing to the γ-radiation from the sample.

Line broadening on powder photographs is mainly caused by : (i) small crystallite size, (ii) thermal motion of the atoms, (iii) structural irregularities, and (iv) composition irregularities. We have endeavoured to diminish the effect of small crystallite size by annealing the specimens where possible for prolonged periods. The second cause is applicable in the present case, as the heat evolved in the stoppage of the α-particles within the sample (27·4 cals. per hr. per c of ^{210}Po) is sufficient to give a temperature of *ca.* 80° at the surface and an internal temperature probably much greater than this. Apart from line broadening the elevated temperature also causes the intensity I_T to be reduced according to the relation $I_o = I_T \exp. -B(\sin\theta/\lambda)^2$, where I_o is the observed intensity and exp. $-B(\sin\theta/\lambda)^2$ is the temperature or Debye factor (Internationale Tabellen, Vol. II, p. 570). For the remaining two causes of line broadening we have insufficient evidence to say whether or not they affect the photographs. However, it seems unlikely that irregularities occur in the composition of compounds such as Cs_2PoBr_6. It would be of interest to repeat the crystallographic studies at low temperatures.

Polonium tetrabromide. Photographs of the tetrabromide were obtained free from the metal, oxide, or dibromide. The diffraction pattern was not similar to that of the tetrachloride (Part I, *loc. cit.*). The pattern was indexed on the basis of a face-centred cubic cell with $a = 5{\cdot}60 \pm 0{\cdot}01$ *kX*, giving a calculated volume of 176 $(kX)^3$. On spatial considerations the cell can only contain one molecule of $PoBr_4$, and hence one atom of polonium. The face-centred cubic space-groups, which contain no one- or two-fold symmetry positions, require a minimum of four Po atoms per unit cell, which is impracticable on spatial considerations. The chemical evidence, which strongly supports a formula $PoBr_4$, is apparently at variance with the crystallographic data.

In order to correlate the *X*-ray crystallographic data with the chemical data two postulates can be made. The first is that the face-centred cubic cell is a pseudo-cell, the true cell being of lower symmetry, and that the lines due to this true cell are extremely weak and therefore not observed on the photographs. The second is that the one polonium atom is randomly distributed over a 4-fold position. With this statistical distribution of the polonium atoms

and the bromine atoms on a 4-fold position the face-centred cubic symmetry would be preserved. This can readily be tested by intensity calculations.

Accordingly, with the polonium atom on the 4(*a*) and the bromine atom on the 4(*b*) special positions of space group O_h^5–$Fm3m$, the intensities I_c, where $I_c \propto F^2m(1 + \cos^2 2\theta)/\sin^2\theta\cos\theta$ (F, m, and the function of θ are respectively the structure factor, multiplicity constant, and the Lorentz polarisation correction factor), were calculated. The following Table shows that the agreement of the observed with the calculated intensities is fair.

hkl	111	200	220	113	222	400	351	420
I_c	9·9	100·0	68·6	2·8	23·7	10·8	1·3	20·0
I_o	vw	s	m	vvw	vw	vvw	—	vvw

The polonium is in octahedral co-ordination with bromine with a Po–Br distance of 2·8 *kX*. The intensities and interatomic distances are not incompatible with the postulate of random distribution of the polonium atoms in the tetrabromide.

Polonium dibromide. Photographs have been obtained of samples free from the tetrabromide, oxide, or metal, but so far attempts to index the diffraction pattern unambiguously have been unsuccessful. The $\sin^2\theta$ values for the stronger lines are recorded in the following Table for identification purposes.

$\sin^2\theta$	0·0176	0·0412	0·0494	0·0682	0·0749	0·1401	0·1602	0·1657
I_o	w+	w+	w+	vw	w+	vw	vw	w−

Ammonium hexabromopolonite. The *X*-ray diffraction photographs were indexed on the basis of a face-centred cubic cell with $a = 10{\cdot}82 \pm 0{\cdot}02$ *kX*. With four molecules per unit cell the calculated density is 3·78 g./c.c. The nitrogen, polonium, and bromine atoms were placed on the special positions 8(*c*), 4(*a*), and 24(*e*), respectively, of space-group O_h^5–$Fm3m$. The variable parameter for the bromine atoms was found from the intensity calculations to be $x = 0{\cdot}24$. The agreement between the observed (I_o) and calculated (I_c) intensities is seen from the following table to be very fair.

hkl	I_o	I_c	*hkl*	I_o	I_c	*hkl*	I_o	I_c	*hk*	I_o	I_c
111	w+	73·8	222	vw	19·3	422	—	0·8	531	—	20·8
200	m	100·0	400	w	59·7	511 }	vvw	19·3	600 }	vvw	24·4
220	—	2·84	331	vw	10·3	333 }			442 }		
113	vw	32·6	420	w−	49·4	440	w	39·5			

The Po–Br distance is 2·60 *kX*, giving a Po^{4+} radius of 0·65, if the ionic radius of bromine is taken as 1·95 showing that the bonding is largely covalent in character. $(NH_4)_2PoBr_6$ is isostructural with $(NH_4)_2PoCl_6$ (Part I, *loc. cit.*).

Cæsium hexabromopolonite. Cs_2PoBr_6 is face-centred cubic with $a = 10{\cdot}99 \pm 0{\cdot}02$ *kX*, and with four molecules per unit cell the density is 4·75 g./c.c. It is isostructural with $(NH_4)_2PoCl_6$ (Part I, *loc. cit.*). The variable parameter for the bromine atoms is $x = 0{\cdot}24$. The agreement between the observed (I_o) and calculated (I_c) intensities is good :

hkl	I_o	I_c	*hkl*	I_o	I_c	*hkl*	I_o	I_c	*hkl*	I_o	I_c
111	m	73	400	m+	100	440	m+	68	620	vvw	12
200	—	10	331	vvw	14	531	vw	30	533	—	5
220	m−	52	420	—	4	600 }	—	1	622	vw	24
311	w−	29	422	w	24	442 }			444	vw	23
222	m	77	511 }	vw	16						
			333 }								

The Po–Br distance is 2·6 *kX*, giving a Po^{4+} radius of 0·69 *kX*. The bonding, as in $(NH_4)_2PoBr_6$, is largely covalent in character.

Cæsium hexabromotellurite. This compound was prepared in order to determine whether the tellurium compound was isostructural with its polonium analogue.

Photographs were obtained by using a Guinier-type focusing camera with a bent quartz crystal monochromator and Cu-$K\alpha$ radiation (D'Eye, A.E.R.E. C/R 1524, S.O.70-674-1-78). In this way $\sin^2\theta$ values were obtained free from absorption and eccentricity errors. By photographing a 0·1-mm. scale on to the film, before processing, shrinkage errors were also eliminated. The expression for the intensity of a line with this camera is $I_c \propto A_1A_2pF^2$ $(1 + \cos^2 2\theta_m \cos^2 2\theta)/(\sin^2\theta\cos\theta)\cos(2\theta - \alpha)$, where I_c is the calculated intensity, θ the Bragg angle, θ_m the angle the *X*-ray beam from the anticathode makes with the monochromator (for Cu, $\theta_m = 13°21'$), A_1 the absorption factor for the specimen, A_2 the absorption factor for film emulsion, p the multiplicity constant, α the angle the beam from the monochromator makes

with the specimen (in our case = 30°), and F the structure factor (Hagg, personal communication); but for cases where the absorption in the specimen is low (in this case because of the extreme thinness of the specimen) and where extreme accuracy is not required the expression simplifies to $I_c \propto pF^2(1 + \cos^2 2\theta m \cos^2 2\theta)/(\sin^2\theta \cos\theta)$ and this expression has been used throughout in calculating the intensities.

Cs_2TeBr_6 was found to be face-centred cubic with $a = 10{\cdot}888 \pm 0{\cdot}005$ kX and has a density of 4·47 g./c.c. The agreement between the observed and calculated $\sin^2\theta$ values is good. The variable parameter for the bromine atom was found to be $x = 0{\cdot}24$.

hkl	$(\sin^2\theta)_o$	$(\sin^2\theta)_c$	I_o	I_c	*hkl*	$(\sin^2\theta)_o$	$(\sin^2\theta)_c$	I_o	I_c
111	0·0149	0·0150	w	29·9	511 } 333 }	1347	1348	w⁻	9·1
200	0199	0200	vvw	0·1					
220	0399	0399	m	34·6	440	1598	1598	s⁻	71·9
311	0547	0549	w	11·4	531	1746	1747	vw	7·2
222	0597	0599	s	100·0	600 } 442 }	—	1797	—	0·0
400	0799	0799	s⁻	99·8					
331	0947	0949	vw	2·3	620	1999	1997	vw	8·1
420	—	0999	—	0·1	533	—	2147	—	1·6
422	1197	1198	w+	15·4	622	2197	2197	m⁻	42·3
					444	2397	2397	w+	25·2

Cs_2TeBr_6 is thus isostructural with Cs_2PoBr_6.

The Te–Br distance is calculated as 2·61 kX, giving a Te^{4+} radius of 0·66 kX. Pauling gives the ionic radius of Te^{4+} as 0·81 kX (Internationale Tabellen, Vol. II) which indicates that the Te–Br bonding in Cs_2TeBr_6 is largely covalent in character.

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Homolytic Aromatic Substitution. Part X. The Phenylation of Pyridine.*

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The proportions of the isomeric phenylpyridines formed in the reaction between pyridine and (*a*) benzoyl peroxide, (*b*) lead tetrabenzoate, (*c*) phenyl iodosobenzoate, (*d*) nitrosoacetanilide, and (*e*) phenylazotriphenylmethane † have been determined. Reactions with (*a*), (*b*), and (*c*) reveal a common mechanism. The reaction with (*e*) gives rise to the formation of a by-product, $C_{30}H_{23}N$, which on infrared spectrometric evidence is regarded as being derived from 2-phenylpyridine. When allowance is made for the disappearance of the 2-isomeride in this manner the results obtained with phenylazotriphenylmethane are quantitatively the same as those obtained with benzoyl peroxide, lead tetrabenzoate, and phenyl iodosobenzoate.

Hey, Nechvatal, and Robinson (*J.*, 1951, 2892) have reviewed the arylation of aromatic compounds by certain diazo-derivatives and aroyl peroxides. These compounds were considered to phenylate by providing free radicals and were divided into five classes. Pyridine has been shown to be phenylated by each class of compound as follows : (*a*) the diazoic acids or diazoates (Mohlau and Berger, *Ber.*, 1893, **26**, 1994; Haworth, Heilbron, and Hey, *J.*, 1940, 349); (*b*) the acylarylnitrosamines (Haworth, Heilbron, and Hey, *J.*, 1940, 372); (*c*) the 1-aryl-3 : 3-dimethyltriazens (Elks and Hey, *J.*, 1943, **441**); (*d*) the arylazotriarylmethanes (Wieland, *Annalen*, 1934, **514**, 145; Adams, Hey, Mamalis, and Parker, *J.*, 1949, 3181; Huisgen and Nakaten, *Annalen*, 1954, **586**, 70); and (*e*) the aroyl peroxides (Overhoff and Tilman, *Rec. Trav. chim.*, 1929, **48**, 993; Hey and Walker, *J.*, 1948,

* Part IX, *J.*, 1955, 1425.

† The well-understood name, phenylazotriphenylmethane, is used here for the compound $PhN{:}N{\cdot}CPh_3$ pending clarification of the nomenclature rules governing this class of compound.

2213; Dannley, Gregg, Phelps, and Coleman, *J. Amer. Chem. Soc.*, 1954, **76**, 445). In addition, Sandin and Brown (*ibid.*, 1947, **69**, 2253) have shown that the decomposition of diphenyliodonium chloride in aqueous alkaline pyridine results in the formation of the three isomeric phenylpyridines. In all of the above reactions a mixture of the isomeric phenylpyridines was isolated from which in some instances one or more of the isomers was isolated, either as such or as a derivative. The only determination of the proportions of each isomer formed on the phenylation of pyridine is that of Dannley *et al.* (*loc. cit.*) who, in the reaction with benzoyl peroxide at 70°, reported 58 ± 3·5% phenylation at the 2-position, 28 ± 3% at the 3-position, and 14 ± 1·5% at the 4-position.

In the present work, five phenylation reactions have been selected for quantitative study, namely, those with benzoyl peroxide, phenylazotriphenylmethane, nitrosoacetanilide, lead tetrabenzoate (Part VI, *J.*, 1954, 2747), and phenyl iodosobenzoate (of which a full discussion is deferred to a later paper). Each of these five compounds has been allowed to decompose in pyridine at 105°, the mixture of isomeric phenylpyridines formed has been isolated quantitatively, and the proportion of the isomers in the mixture determined by means of ultraviolet spectroscopy. The results of these experiments are shown in Table 2 below. Further, the presence of all three isomers in the mixtures obtained from the reactions with lead tetrabenzoate and phenyl iodosobenzoate was demonstrated by conversion of the mixtures into the picrates, fractional crystallisation of which yielded each isomer as its pure picrate (cf. Haworth, Heilbron, and Hey, *loc. cit.*).

The ratios of isomerides obtained in the experiments with benzoyl peroxide, lead tetrabenzoate, and phenyl iodosobenzoate are in good agreement (Table 2) and it is clear that the mechanism of the decomposition, which comprises an initial breakdown to benzoyloxy-radicals and hence, by loss of carbon dioxide, to phenyl radicals, is common to each reaction.

From the reaction of phenylazotriphenylmethane with pyridine a compound, $C_{30}H_{23}N$, m. p. 215°, was isolated in 28% yield in addition to the phenylpyridines and tri- and tetraphenylmethane. Huisgen and Nakaten (*loc. cit.*) also isolated this compound in the same yield from the products of this reaction and suggested that it was a triphenylmethyl-substituted phenylpyridine. Oxidation of this compound with acid and with alkaline permanganate (cf. Tschitschibabin, *Ber.*, 1904, **37**, 1373; Skraup and Cobenzl, *Monatsh.*, 1883, **4**, 436) yielded no information. The infrared spectrum of the compound showed a band at 842 cm.$^{-1}$, characteristic of a *para*-disubstituted benzene nucleus (cf. earlier papers in this series), and bands at 1272 and 1185 cm.$^{-1}$. Absorption at these wavelengths has been reported in compounds containing a triphenylmethyl group (Pinchas and Samuel, *J.*, 1954, 863). The latter pair of bands was, however, shown also to be present in the spectra of 2-, 3-, and 4-phenylpyridine. Each band in the spectrum of the compound, m. p. 215° (except for that at 842 cm.$^{-1}$), could be accounted for by taking the spectrum of 2-phenylpyridine in conjunction with that of tetraphenylmethane, whereas this result could not be achieved (see Experimental section) by substituting the spectrum of either 3- or 4-phenylpyridine for that of the 2-isomer. The ratio of isomerides was therefore recalculated (Table 2) on the assumption that the phenylpyridine consumed in the formation of the compound, m. p. 215°, was the 2-isomer. The corrected values for the ratio of isomerides are found to be close to those obtained with benzoyl peroxide, lead tetrabenzoate, and phenyl iodosobenzoate.

The foregoing evidence suggests that the compound, m. p. 215°, may be *p*-2-pyridyltetraphenylmethane. An attempt to synthesise *p*-2-pyridyltetraphenylmethane by a Wurtz–Grignard reaction between 2-*p*-bromophenylpyridine and triphenylchloromethane failed, as 2-*p*-bromophenylpyridine did not react with magnesium. A second attempt was made by a route analogous to that used for the synthesis of 2-phenylpyridine (Ziegler and Zeiser, *Ber.*, 1930, **63**, 1847). *p*-Triphenylmethylphenyl-lithium was prepared by the reaction of *n*-butyl-lithium with *p*-bromotetraphenylmethane. The product, on treatment with pyridine and subsequent heating at 110°, yielded a compound $C_{30}H_{23}N$, m. p. 215°, which, however, depressed the melting point of the compound of the same melting point isolated from the reaction of phenylazotriphenylmethane with pyridine. The possibility that the compound synthesised was the 1 : 2-dihydro-derivative was rejected because the

compound was unaffected on treatment with palladium on charcoal. In spite of the failure to synthesise the compound obtained from the phenylazotriphenylmethane reaction, the spectral evidence, which shows that it is the 2-phenylpyridine which is consumed in the formation of the compound, $C_{30}H_{23}N$, is considered to justify the correction made to the ratio of isomerides.

In the reaction with nitrosoacetanilide only 47% of the starting material was accounted for, and much intractable tar was formed. It is probable that side reactions affecting individual isomers account for the anomalous values of the isomer ratio which are obtained, and little significance is attached to them. The ratios of isomerides obtained in the reactions of pyridine with benzoyl peroxide, lead tetrabenzoate, and phenyl iodosobenzoate are, however, the same within the limits of the accuracy of the determination, and moreover, that obtained in the phenylazotriphenylmethane reaction, after correction for the effect of a subsequent reaction on the 2-phenylpyridine, has a similar value. In a detailed investigation of the kinetics of the decomposition of phenylazotriphenylmethane, Huisgen and Nakaten (*loc. cit.*) have been able to distinguish between (*a*) a simple dissociation into free radicals, (*b*) a free-radical chain decomposition, and (*c*) the formation of a complex with the solvent before dissociation, followed by a directed radical reaction. Their results, which favour mechanism (*a*), taken in conjunction with the results that we have obtained, make it seem likely that the phenylating agent is the same in all these reactions, and that it is, in fact, the phenyl radical.

The value for the ratio of isomerides obtained in the benzoyl peroxide reaction, taken in conjunction with the rate of substitution relative to benzene (Augood, Hey, and Williams, *J.*, 1952, 2094), gives the following partial rate factors for the phenylation of pyridine: 2-position, 1·69; 3-position, 1·0; 4-position, 0·87. Yvan's calculation (*Compt. rend.*, 1949, **229**, 622) of what are termed " potential barriers " for radical substitution in pyridine are in qualitative agreement with these values (cf. Hey and Williams, *Discuss. Faraday Soc.*, 1953, **14**, 216).

Experimental

Reagents.—Pyridine (Hopkins and Williams, AnalaR) was dried (KOH) and fractionally distilled (b. p. 115·5°/750 mm.). It was redistilled from anhydrous barium oxide immediately before use. 5-Ethyl-2-methylpyridine (Light) was fractionally distilled and collected at 78°/22 mm. (picrate, m. p. 167°). Benzoyl peroxide (May and Baker) was purified according to the procedure described by Augood, Hey, and Williams (*loc. cit.*).

Reactions in Pyridine.—The following series of reactions was carried out in duplicate in a thermostat maintained at 105° ± 0·1°. The method used was that of Augood, Hey, and Williams (*loc. cit.*). In each case the concentration of the phenylating agent was 1 mole per 55 moles of pyridine. In each of the first three reactions the reagent was added rapidly to the pyridine at 105°. The mixtures were removed from the thermostat after 20 hr. except in the case of phenyl iodosobenzoate, when heating was continued for 60 hr.

(a) *With benzoyl peroxide* (5·25 g./100 ml. of pyridine). After the reaction was complete, pyridine was removed by distillation through a 25-cm. helix-packed column, and esters in the residue were hydrolysed by boiling for 4 hr. with 2N-sodium hydroxide (100 ml.). The unsaponifiable material was thoroughly extracted with benzene (5 × 30 ml.). The benzene extracts were then extracted with 7N-hydrochloric acid (3 × 50 ml.), and the acid extracts were neutralised by the addition of excess of concentrated aqueous sodium hydroxide. The alkaline solution was extracted with benzene (5 × 30 ml.), and the extracts dried ($CaCl_2$). Benzene was removed by distillation through a 25-cm. helix-packed column and the residue was distilled at reduced pressure to give an oil (2·08 g.), b. p. 139—141°/12 mm., which partly solidified. The residue weighed 0·27 g.

(b) *With lead tetrabenzoate* (Hey, Stirling, and Williams, *loc. cit.*; 18·0 g./120 ml. of pyridine). The working procedure was that described for benzoyl peroxide, except that, after the removal of pyridine, lead benzoate was precipitated by the addition of light petroleum (b. p. 60—80°; 100 ml.) and filtered off. Light petroleum was removed from the filtrate by distillation and the residue was treated with sodium hydroxide as before. The final distillation yielded an oil (1·65 g.), b. p. 140—144°/12 mm., and a residue (0·080 g.).

(c) *With phenyl iodosobenzoate* (14·49 g./150 ml. of pyridine). The preparation of this compound, m. p. 159·5—160·5° (Found: C, 53·8; H, 3·3%; equiv., 223. Calc. for $C_{20}H_{15}O_4I$: C,

53·8; H, 3·4%; equiv., 223) from iodosobenzene by a modification of Arbuzov's method (*J. prakt. Chem.*, 1931, **131**, 357) will be described fully in a later paper. The working-up procedure was the same as for the benzoyl peroxide reaction. Iodobenzene was isolated in almost quantitative yield from the benzene extracts of the mixture after treatment with sodium hydroxide and removal of the basic components by acid extraction. The final distillation gave an oil (1·17 g.), b. p. 138°/10 mm., and a residue (0·084 g.).

(d) *With nitrosoacetanilide* (France, Heilbron, and Hey, *J.*, 1940, 369; 3·56 g./100 ml. of pyridine). The reagent was dissolved in pyridine (25 ml.) which had previously been cooled to −20°, and the solution was added dropwise to the remainder of the pyridine at 105°. The working-up procedure was the same as for the benzoyl peroxide reaction, and final distillation gave a yellow oil (1·59 g.), b. p. 137°/10 mm., from which the colour was not removed by chromatography, and a residue (0·48 g.).

(e) *With phenylazotriphenylmethane* (Wieland, Hove, and Börner, *Annalen*, 1926, **446**, 31; 12·55 g./166 ml. of pyridine). The reagent was dissolved in 161 ml. of pyridine at room temperature and the solution was added dropwise during 2 hr. to the remainder of the pyridine at 105°. After 20 hr. the pyridine was removed by distillation and chloroform (100 ml.) was added to the residue. The chloroform solution was extracted with 7N-hydrochloric acid (4 × 15 ml.), washed with water, and dried ($CaCl_2$). The acid extracts were worked up in the manner described for the benzoyl peroxide reaction, yielding an oil, b. p. 130°/8 mm. (2·20 g.), and residue (0·06 g.). The chloroform solution was evaporated to dryness and the residue (10·22 g.), after extraction successively with (*a*) boiling light petroleum (b. p. 40—60°; 50 ml.) and (*b*) ether (60 ml.), left a pale-brown residue (*c*). Both extracts were evaporated to dryness and the three residues were chromatographed on alumina. Residue from (*a*) (7·00 g.) yielded triphenylmethane (4·6 g.), m. p. and mixed m. p. 92°, and a compound, $C_{36}H_{23}N$ (m. p. 215°; 0·49 g.) (see below). Residue from (*b*) (1·70 g.) yielded chiefly the compound, m. p. 215° (1·14 g.), and a small amount of tetraphenylmethane (0·10 g.), m. p. and mixed m. p. 275°. Residue (*c*) (1·32 g.) yielded the compound, m. p. 215° (1·12 g.), and tetraphenylmethane (0·04 g.). In this way 75% of the neutral residue was accounted for. The compound, m. p. 215°, is believed to be isolated quantitatively as a result of its very sparing solubility in light petroleum (b. p. 40—60°).

The other products isolated from this series of reactions are listed in Table 1. Benzoic acid, which was formed in the first three reactions, was isolated by the following procedure. The alkaline extracts obtained after the hydrolysis stage of the working-up procedure were made just acid with concentrated hydrochloric acid, neutralised by the addition of solid sodium hydrogen carbonate, and filtered. The filtrate was extracted with methylene chloride and acidified with concentrated hydrochloric acid, and the precipitated benzoic acid was quantitatively extracted with methylene chloride (4 × 30 ml.). The aqueous layer was rejected and the combined methylene chloride extracts, after being dried (Na_2SO_4), were evaporated at room temperature. The residual benzoic acid had m. p. and mixed m. p. 117—119°. In this series of reactions no identifiable products could be isolated from the residues obtained after distillation of the phenylpyridines. They probably consisted mainly of higher phenylated products. They have not been included in the calculations of the proportions of the phenyl radicals accounted for in each reaction.

TABLE 1. *Products obtained in reactions with pyridine at* 105°

Reagent	$Ph{\cdot}CO_2H$, mol.*	$Ph{\cdot}C_5H_4N$, mol.*	% Ph accounted for
Benzoyl peroxide	0·89	0·62	76
Lead tetrabenzoate	1·16	0·42	78
Phenyl iodosobenzoate	1·66	0·23	95
Nitrosoacetanilide	—	0·47	47
Phenylazotriphenylmethane	—	0·40	61

* Per mol. (mean) of reagent.

The isomer ratios of the products formed in these reactions were determined by ultraviolet spectrophotometry with the aid of a "Unicam S.P. 500" quartz spectrometer. The method of calculation previously described (Cadogan, Hey, and Williams, *J.*, 1954, 794) was used. The solvent was ethanol.

The absorption curves of the isomeric phenylpyridines have been recorded by Gillam, Hey, and Lambert (*J.*, 1941, 366). The pure isomers for the calibration spectra were obtained from their picrates (cf. Haworth, Heilbron, and Hey, *loc. cit.*). The picrates of 2- and 3-phenylpyridine (m. p. 176° and 160°, respectively) were chromatographed on alumina in methylene chloride solution. Removal of methylene chloride from the eluates, and distillation of the

residue gave 2-phenylpyridine, b. p. 127°/8 mm., n_D^{20} 1·6227, and 3-phenylpyridine, b. p. 141°/12 mm., n_D^{20} 1·6143. 4-Phenylpyridine (plates, m. p. 73°, from water) was obtained by treatment of the pure picrate, m. p. 197°, with 10% aqueous sodium hydroxide.

The extinction coefficients of the mixtures from the duplicate reactions with benzoyl peroxide, phenyl iodosobenzoate, lead tetrabenzoate, and nitrosoacetanilide differed only slightly from each other, and mean values were used for purposes of calculation. The mixtures from the phenylazotriphenylmethane reactions were treated separately. As the method of calculation is valid only for mixtures which contain only the three isomers, the nitrogen content of each mixture was determined (Calc. for $C_{11}H_9N$: N, 9·05%). The compositions of the mixtures thus obtained are given in Table 2, the overall error in each determination being ±2%.

TABLE 2 *Ratios of isomerides obtained in the phenylation of pyridine at* 105°

Reagent	Isomers, % 2-	3-	4-	N, %
Benzoyl peroxide	54	32	14	(1) 9·35, (2) 9·00
Lead tetrabenzoate	52	32·5	15·5	(1) 9·15, (2) 8·80
Phenyl iodosobenzoate	58	28	14	(1) 9·18, (2) 9·25
Nitrosoacetanilide	46	43	11	(1) 8·90, (2) 9·35
Phenylazotriphenylmethane	(1) 29·3	47	23·7	8·94
,,	(2) 30·6	46·4	23	9·20
,, (corrected)	53	31	16	—

The compound, m. p. 215° (Found: C, 90·6; H, 5·9; N, 3·35%; *M*, 342. Calc. for $C_{36}H_{23}N$: C, 90·7; H, 5·8; N, 3·5%; *M*, 397). Huisgen and Nakaten (*loc. cit.*) reported m. p. 213° for this compound. Attempted oxidation with alkaline permanganate resulted in the recovery of starting material in almost quantitative yield. Acid permanganate was decolorised and only part of the starting material was recovered, but no identifiable oxidation products could be isolated.

Infrared Spectra.—The instrument used was a Grubb-Parsons single-beam infrared spectrometer. 2- and 3-Phenylpyridine and 5-ethyl-2-methylpyridine were used as capillary films, and the other compounds investigated as crystalline powders in Nujol mulls, all between rock-salt plates. The spectra of 2-, 3-, and 4-phenylpyridine, 2-*p*-bromophenylpyridine, tetraphenylmethane, *p*-2-pyridyltetraphenylmethane, and the compound of m. p. 215° isolated from the phenylazotriphenylmethane reaction, were taken between 1320 cm.$^{-1}$ and 780 cm.$^{-1}$. Apart from a weak band at 944 cm.$^{-1}$ all the bands in the spectrum of the compound, m. p. 215°, are accounted for by bands in the spectra of 2-phenylpyridine, 2-*p*-bromophenylpyridine or tetraphenylmethane. On the other hand, the spectra of 3- and 4-phenylpyridine show strong absorption bands at 810 and 826 cm.$^{-1}$, respectively, while there is no band in the spectrum of the compound, m. p. 215°, which corresponds to either of these bands. Further, the spectra of these two isomers show no absorption at 1290 and 1089 cm.$^{-1}$, whereas at these wavelengths there are bands of medium intensity in the spectrum of the compound, m. p. 215°. The presence of a band at 844 cm.$^{-1}$ in the spectrum of 2-*p*-bromophenylpyridine confirms that this absorption is characteristic of a *para*-disubstituted benzene nucleus. No band is present at 844 cm.$^{-1}$ in the spectrum of 5-ethyl-2-methylpyridine. This absorption is therefore not due to the presence of a 2 : 5-disubstituted pyridine derivative. A very weak band at 840 cm.$^{-1}$ in the spectrum of tetraphenylmethane is probably due to a trace of *p*-ethoxytetraphenylmethane, formed as a by-product in the preparation of this compound. These results are tabulated in Table 3.

Tetraphenylmethane, m. p. 276°, was prepared by the deamination of *p*-aminotetraphenylmethane by Ullmann and Munzhuber's method (*Ber.*, 1903, **36**, 404).

2-p-*Bromophenylpyridine* (cf. Butterworth, Heilbron, and Hey, *J.*, 1940, 355).—A solution of *p*-bromo-*N*-nitrosoacetanilide (60 g.), prepared by the method of Hey, Stuart-Webb, and Williams (*J.*, 1952, 4657) in anhydrous pyridine (550 ml.), was warmed on the water-bath until the evolution of nitrogen slackened, and was thereafter boiled under reflux for 3 hr. Pyridine was distilled off and the residue dissolved in benzene (150 ml.). The benzene solution was extracted with 7N-hydrochloric acid (5 × 40 ml.). The acid extracts were made alkaline by the addition of excess of aqueous sodium hydroxide and extracted with ether (3 × 100 ml.). Evaporation of the extracts and distillation of the residue yielded a mixture of the isomeric *p*-bromophenylpyridines (19·6 g.), b. p. 135—165°/0·5 mm. This mixture was converted into the mixture of picrates (46 g.), fractional crystallisation of which from acetone yielded 2-*p*-bromophenylpyridine picrate (4·0 g.), m. p. 164°. This picrate was chromatographed in acetone solution on alumina. Evaporation of the eluates and crystallisation of the residue from light

petroleum (b. p. 40—60°) gave 2-*p*-bromophenylpyridine, m. p. 61—62°, in white flakes (1·25 g.). 2-*p*-Bromophenylpyridine did not appear to react with magnesium and from an attempt to couple it with triphenylchloromethane, by Schoepfle and Trepp's method (*J. Amer. Chem. Soc.*, 1932, **54**, 4059), starting material was obtained in quantitative yield.

TABLE 3. *Infrared absorption bands* (*cm.*$^{-1}$).

(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*f*)	(*g*)
1318 m	—	—	—	1308 w	1308 w	1309 w
—	1303 m	—	—	—	—	—
1298 m	—	—	1290 m	—	—	—
1272 m	1275 w	—	1265 w	1273 w	1273 vw	1265 w
1237 w	—	—	1234 vw	1235 vw	1228 vw	—
1185 s	1190 s	1185 m	1183 w	1190 m	1190 vw	1190 w
1153 m	1155 m	—	1150 m	1157 vw	1160 vw	1165 m
—	1121 w	—	—	1123 w, 1105 w	1100 w	1125 w
1089 m	1089 m	—	1092 w	—	—	1103 m
1075 m	—	1075 m	—	1075 m	1070 m	1075 m
—	1065 w	—	1063 m	—	—	—
—	—	—	—	1051 vw	—	—
1038 s	1038 s	—	—	—	1040 vw	1038 w
—	—	1030 m	—	—	—	—
1020 m	1020 s	—	1020 m	1020 s	—	—
—	—	—	—	—	—	1010 m
1002 m	1000 m	995 m	—	1002 vs	995 w	—
990 w	990 w	980 w	985 m	990 m	985 w	990 m
—	—	—	—	—	962 vw	—
944 w	944 w	—	—	948 vw	—	—
934 w	—	935 w	—	—	—	—
921 w	—	—	916 w	—	915 m	—
—	—	—	—	909 m	—	—
893 m	893 m	889 w	882 vw	—	—	—
—	—	855 vw	—	—	865 vw	—
842 vs	840 s	840 vw	—	—	—	844 s
—	—	—	—	810 vs	826 vs	—
—	—	—	796 m	—	—	—
781 m	—	—	—	—	—	—

(*a*) Compound, m. p. 215°, isolated from phenylazotriphenylmethane reaction. (*b*) *p*-2-Pyridyltetraphenylmethane. (*c*) Tetraphenylmethane. (*d*) 2-Phenylpyridine. (*e*) 3-Phenylpyridine. (*f*) 4-Phenylpyridine. (*g*) 2-*p*-Bromophenylpyridine.

w = weak. m = medium. s = strong. v = very.

p-*Bromotetraphenylmethane*.—*p*-Aminotetraphenylmethane (25 g.), prepared by Ullmann and Munzhuber's method (*loc. cit.*) was heated to boiling with glacial acetic acid (150 ml.). The suspension was cooled and constant-boiling (48%) hydrobromic acid (12 ml.) was added. Amyl nitrite (18 ml.) was added dropwise to the vigorously stirred suspension of the hydrobromide. After 2 hr. the mixture was filtered and ether (1 l.) was added to the filtrate. The pale grey diazonium bromide was filtered off, dried *in vacuo* (17 g.), and added in portions, with stirring, to a boiling solution of cuprous bromide (17 g.) in 48% hydrobromic acid (200 ml.). The mixture was diluted with water to 1 l. and filtered. The residue was washed with 48% hydrobromic acid (50 ml.), water, and methyl alcohol (200 ml.). The crude *p*-bromotetraphenylmethane (17 g.), after purification by chromatography in benzene solution on alumina, had m. p. 245°. Schoepfle and Trepp (*loc. cit.*) reported m. p. 246° for this compound.

p-2-*Pyridyltetraphenylmethane*.—A solution of *n*-butyl-lithium (Gilman, Beel, Brannen, Bullock, Dunn, and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 1499) was prepared from lithium (0·8 g.) and *n*-butyl bromide (6·8 g.) in anhydrous ether (30 ml.). *p*-Bromotetraphenylmethane (4 g.) and anhydrous ether (50 ml.) were then added to the ethereal solution of *n*-butyl-lithium. The resulting suspension was boiled for 2 hr., the bromo-compound having then dissolved to give a clear solution. Anhydrous pyridine (15 ml.) in toluene (60 ml.) was added with stirring and cooling to the solution of *p*-triphenylmethylphenyl-lithium. The mixture was distilled until the boiling point reached 110° and was then stirred at 110° for 8 hr. After the mixture had cooled to room temperature, water (150 ml.) was cautiously added and the mixture was filtered. The organic layer was separated and chloroform (150 ml.) was added. The solution was extracted with 5N-hydrochloric acid (120 ml.), washed with water, and dried ($CaCl_2$). Chloroform was removed and the residue was chromatographed in benzene solution on alumina. The eluates yielded p-2-*pyridyltetraphenylmethane* (2·9 g.), m. p. 215°, in needles from benzene–light

petroleum (b. p. 80—100°) (Found: C, 90·5; H, 6·1. $C_{30}H_{23}N$ requires C, 90·7; H, 5·8%). This compound was unaffected by boiling a nitrobenzene solution for 1 hr. and was recovered quantitatively. A solution of 1 g. of the compound in *p*-cymene (100 ml.), to which 5% palladium on charcoal (1·5 g.) was added, was distilled until the reflux temperature reached 175° and heating was continued under reflux for 2 hr. (cf. Walker, *J. Amer. Chem. Soc.*, 1954, **76**, 3999). The hot mixture was filtered and a further 1·5 g. of catalyst was added. The mixture was again distilled until the boiling point rose to 175°, and was boiled for a further 2 hr. The catalyst was filtered off and *p*-cymene was removed by steam-distillation. Recrystallisation of the residue from benzene–light petroleum (b. p. 80—100°) gave starting material (m. p. and mixed m. p. 215°).

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The Isomerization of αβ-Di(arylhydrazono)-γ-butyrolactones.

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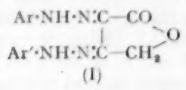
The lactone osazones (I) are converted by hot alkali into 1-aryl-4-arylazo-3-hydroxymethylpyrazol-5-ones (II; R = H). Reduction of the pyrazolone (II; Ar = Ar′ = Ph, R = H) gives 4-amino-3-hydroxymethyl-1-phenylpyrazol-5-one (IV; Y = OH) which is oxidized by ferric chloride to the substituted rubazonic acid (V; Y = OH).

WOLFF and LÜTTRINGHAUS (*Annalen*, 1900, **312**, 155) reported that a dihydrazone (I; Ar = Ar′ = Ph) with hot alcoholic alkali gave an alkali-soluble yellow compound which was not examined and for which no structure was postulated. Investigation of the pure compound has shown that it is isomeric with the dihydrazone and although soluble in aqueous sodium hydroxide is insoluble in aqueous sodium carbonate, indicating that it has weakly acidic properties. With acetic anhydride it gives a monoacetyl derivative which is soluble without decomposition in aqueous sodium hydroxide, and on reduction it gives aniline and a basic compound isolated as the hydrochloride. This hydrochloride is also obtained, together with *p*-chloroaniline, by reduction of the corresponding isomer (I; Ar = *p*-chlorophenyl, Ar′ = Ph), showing that, in the isomer, it is only the hydrazono-group originally in the α-position of the osazone which undergoes reduction. It is suggested, therefore, that of two possible isomers (II; Ar = Ar′ = Ph, R = H) and (III), Wolff and Lüttringhaus's compound is the former, whilst its acetyl derivative and reduction product have structures (II; Ar = Ar′ = Ph, R = Ac) and (IV; Y = OH) respectively.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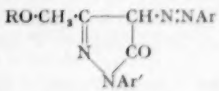
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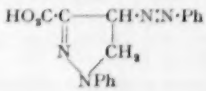
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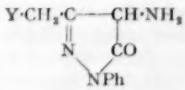
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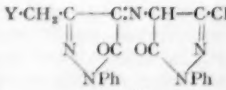
(V)

Confirmation of the structure (IV; Y = OH) and therefore of (II) is given by the similarity of the behaviour of the former compound to 4-amino-3-methyl-1-phenylpyrazol-5-one (IV; Y = H) on oxidation with ferric chloride. The oxidation product (V; Y = OH), like rubazonic acid (V; Y = H), is purple in alkaline solution and with

phenylhydrazine in acetic acid gives the pyrazolone (II; Ar = Ar′ = Ph, R = H) (cf. Knorr, *Annalen*, **1887**, **238**, 189).

Experimental

β-Oxo-α-phenylhydrazono-γ-butyrolactone.—The following procedure avoids the tedious isolation of tetronic acid. α-Ethoxycarbonyl-β-oxo-γ-butyrolactone (17·2 g.) (Benary, *Ber.*, 1907, **40**, 1080) was dissolved in 12% aqueous sodium hydroxide (100 ml.) and left for 60 hr. at 18°. Concentrated hydrochloric acid (30 ml.) was added, the temperature rising to 42° and carbon dioxide being evolved. After 1 hr. potassium carbonate (25 g.) was added and the solution cooled to 0°. Benzenediazonium chloride [from aniline (9·0 ml.), 5N-hydrochloric acid (50 ml.), and sodium nitrite (7·5 g.) in water (30 ml.)] was added at 0—2°. After 1 hr. at 0°, the resulting yellow precipitate was filtered off, washed with water, dried *in vacuo*, and recrystallized from chloroform to give β-oxo-α-phenylhydrazono-γ-butyrolactone as yellow leaflets, m. p. 210° (12·8 g., 58%), identical with the compound obtained from tetronic acid (Wolff and Lüttringhaus, *loc. cit.*). Similarly were prepared *β-oxo-α-o-tolylhydrazono-γ-butyrolactone*, yellow needles (from ethanol), m. p. 160° (48%) (Found: C, 60·5; H, 4·7. $C_{11}H_{10}O_3N_2$ requires C, 60·6; H, 4·6%), and α-o-, yellow needles (from ethanol), m. p. 158° (62%) (Found: C, 50·4; H, 3·0; Cl, 14·7. $C_{10}H_7O_3N_2Cl$ requires C, 50·3; H, 2·94; Cl, 14·9%), and α-p-*chlorophenylhydrazono-β-oxo-γ-butyrolactone*, orange needles (from acetic acid), m. p. 228·5° (decomp.) (75%) (Found: C, 50·5; H, 3·0; Cl, 15·0. $C_{10}H_7O_3N_2Cl$ requires C, 50·3; H, 2·95; Cl, 14·9%).

αβ-Di(phenylhydrazono)-γ-butyrolactone was prepared by the method of Wolff and Lüttringhaus (*loc. cit.*) and the following derivatives similarly: *αβ-di-(o-tolylhydrazono)-*, red needles (from ethanol), m. p. 166—167° (68%) (Found: C, 66·8; H, 5·7; N, 17·4. $C_{18}H_{18}O_2N_4$ requires C, 67·2; H, 5·6; N, 17·4%), *αβ-di-(o-chlorophenylhydrazono)-*, bright orange-red plates (from acetic acid), m. p. 220° (84%) (Found: C, 53·15; H, 3·5; Cl, 19·45. $C_{16}H_{12}O_2N_4Cl_2$ requires C, 52·85; H, 3·3; Cl, 19·55%), and α-p-*chlorophenylhydrazono-β-phenylhydrazono-γ-butyrolactone* (from acetic acid), orange leaflets, m. p. 251° (decomp.) (79%) (Found: Cl, 10·9. $C_{16}H_{13}O_2N_4Cl$ requires Cl, 10·8%).

3-Hydroxymethyl-1-phenyl-4-phenylazopyrazol-5-one.—αβ-Di(phenylhydrazono)-γ-butyrolactone (27·5 g.), ethanol (1 l.), and 40% aqueous sodium hydroxide (25 ml.) were heated at 100° for 5 min., the initially purple solution becoming deep yellow. Water (500 ml.) was added and the ethanol removed by distillation. The solution was cooled, filtered from a tarry impurity, and acidified with concentrated hydrochloric acid (25 ml.) to give a yellow precipitate which was filtered off and recrystallized from ethanol. This afforded *3-hydroxymethyl-1-phenyl-4-phenylazopyrazol-5-one* as orange-yellow needles, m. p. 155° (19·1 g., 70%) (Found: C, 65·2; H, 4·8; N, 19·1. $C_{16}H_{14}O_2N_4$ requires C, 65·3; H, 4·75; N, 19·05%). The following analogues were obtained similarly: *4-p-chlorophenylazo-3-hydroxymethyl-1-phenylpyrazol-5-one*, orange-red needles (from ethanol), m. p. 186° (54%) (Found: C, 54·4; H, 4·1; Cl, 10·7. $C_{16}H_{13}O_2N_4Cl$ requires C, 54·5; H, 3·95; Cl, 10·8%); *3-hydroxymethyl-1-o-tolyl-4-o-tolylazopyrazol-5-one* (from ethanol), orange-yellow needles, m. p. 149° (4%) (Found: C, 67·0; H, 5·7. $C_{18}H_{18}O_2N_4$ requires C, 67·2; H, 5·6%); and *1-o-chlorophenyl-4-o-chlorophenylazo-3-hydroxymethylpyrazol-5-one* (from ethanol), yellow leaflets, m. p. 203° (decomp.) (68%) (Found: C, 53·15; H, 3·4. $C_{16}H_{12}O_2N_4Cl_2$ requires C, 52·85; H, 3·3%).

3-Acetoxymethyl-1-phenyl-4-phenylazopyrazol-5-one.—The compound (II; Ar = Ar′ = Ph, R = H) (1·0 g.) and acetic anhydride (5 ml.) were boiled for 5 min., then diluted with water (30 ml.), and the precipitated solid recrystallized from ethanol, to give the *acetoxy-compound* as orange-yellow plates, m. p. 131° (0·65 g., 53%) (Found: C, 64·3; H, 5·0. $C_{18}H_{16}O_3N_4$ requires C, 64·3; H, 4·75%).

Reduction of the Compound (II; Ar = Ar′ = Ph, R = H).—3-Hydroxymethyl-1-phenyl-4-phenylazopyrazol-5-one (2·0 g.), ethanol (20 ml.), 10N-hydrochloric acid (10 ml.), and granulated tin (5 g.) were boiled under reflux; a vigorous reaction occurred and the solution became colourless. The solution was filtered, the filtrate diluted with water, ethanol distilled off, and tin removed from the boiling solution with hydrogen sulphide. Concentration to 20 ml. gave, after 20 hr. at 0°, colourless crystals which recrystallized from 5N-hydrochloric acid to give *4-amino-3-hydroxymethyl-1-phenylpyrazol-5-one hydrochloride* (cf. IV; Y = OH) as needles, m. p. 201—203° (0·92 g., 65%) (Found: C, 49·6; H, 4·9; Cl, 14·8. $C_{10}H_{12}O_2N_3Cl$ requires C, 49·8; H, 5·01; Cl, 14·7%). The combined acid filtrates were basified and steam-distilled to give aniline, which was converted into acetanilide (84%). Reduction of *4-p*-chlorophenylazo-3-hydroxymethyl-1-phenylpyrazol-5-one under similar conditions gave the identical amine hydrochloride (70%) and *p*-chloroacetanilide (79%).

Oxidation of the Pyrazolone (IV; Y = OH).—The amine hydrochloride (0·5 g.) from the above reduction in water (10 ml.) was warmed for 5 min. on the water-bath with 10% aqueous ferric chloride (10 ml.). The orange crystalline precipitate, after filtration and recrystallization from ethanol, gave *3-hydroxymethyl-4-(3-hydroxymethyl-1-phenylpyrazol-5-on-4-ylidene)amino-1-phenylpyrazol-5-one* (V; Y = OH) as orange needles, m. p. 199° (0·38 g., 92%) (Found: C, 61·5; H, 4·2. $C_{20}H_{17}O_4N_5$ requires C, 61·3; H, 4·35%).

The product (V; Y = OH) (0·5 g.), acetic acid (5 ml.), and phenylhydrazine (1·0 ml.) were boiled under reflux for 5 min. and then diluted with water. Recrystallization of the precipitated solid gave the pyrazolone (II; Ar = Ar′ = Ph, R = H) (0·37 g., 50%).

Conversion of the pyrazolone (II; Ar = *p*-chlorophenyl, Ar′ = Ph, R = H) into the same product (V; Y = OH) was also carried out without the isolation of the material (IV; Y = OH) by the following procedure: Zinc dust (5·0 g.) was added gradually to 4-*p*-chlorophenylazo-3-hydroxymethyl-1-phenylpyrazol-5-one (2·0 g.) in acetic acid (10 ml.) and ethanol (50 ml.) on a steam-bath. When colourless the mixture was filtered and diluted with water (100 ml.), ethanol removed, and the residue made alkaline with sodium hydroxide. After ether-extraction the alkaline solution was acidified with 10N-hydrochloric acid, 10% aqueous ferric chloride (15 ml.) added, and the mixture warmed on the steam-bath for 5 min., to give the rubazonic acid (V; Y = OH) (68%). From the ether-extracts, *p*-chloroaniline was isolated and identified as *p*-chloroacetanilide (91%).

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Renwick Laboratory, Ilford Limited, Ilford. [*Received, June 27th*, 1955.]

Constituents of the Lipids of Tubercle Bacilli. Part VI. Phthiocerol.*

By J. A. Hall, J. W. Lewis, and N. Polgar.

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Phthiocerol, a lævorotatory alcohol from the lipids of tubercle bacilli, is shown to afford a benzylidene derivative, thus indicating a 1 : 2- or 1 : 3-glycol structure. Oxidative degradation yields *n*-tetracosanoic acid and a C_{11} methoxy-acid, and the main structural features of phthiocerol in the light of these findings (cf. Hall and Polgar, *Chem. and Ind.*, 1954, 1293, where a preliminary account was given) are discussed. The results of further studies of phthiocerol, including debromination of its dibromo-derivative, and a mild oxidation giving rise to a β-diketone, disclose the presence of a 1 : 3-diol system, and evidence is presented which indicates that a methyl and a methoxyl group are both attached at $C_{(4)}$. It is concluded that phthiocerol is 4-methoxy-4-methyl-*n*-tetratriacontane-9 : 11-diol (V).

Phthiocerol, $[\alpha]_D$ −4·8°, m. p. 73—74°, isolated from the lipids of human and bovine tubercle bacilli (Stodola and Anderson, *J. Biol. Chem.*, 1936, **114**, 467; Reeves and Anderson, *ibid.*, 1937, **119**, 535; Cason and Anderson, *ibid.*, p. 549), was shown by the first-named authors to have the empirical formula $C_{35}H_{72}O_3$ or $C_{36}H_{74}O_3$, and to contain two hydroxyl and one methoxyl group. Contrary to earlier statements (cf. Reeves and Anderson, *J. Amer. Chem. Soc.*, 1937, **59**, 858), the same alcohol was recently found in the lipids of avian tubercle bacilli (Hall and Polgar, unpublished work); it is probably essentially the "phtioglycol" of Stendal (*Compt. rend.*, 1934, **198**, 1549). From the properties exhibited by monolayers of phthiocerol Ställberg and Stenhagen (*J. Biol Chem.*, 1942, **143**, 171) inferred that it contains a long carbon chain with one or more of the polar groups near one end. Reaction of phthiocerol with hydriodic acid and reduction of the resulting iodo-derivative with zinc and acetic acid gave a product which was partly unsaturated and on catalytic hydrogenation, followed by treatment with hot concentrated sulphuric acid, afforded a saturated hydrocarbon, phthiocerane (Stodola and Anderson, *loc. cit.*; Ginger and Anderson, *J. Biol. Chem.*,

* The paper by Marks and Polgar, *J.*, 1955, 3851, is regarded as Part V.

1945, **157**, 213), containing, according to infrared studies, a methyl branch at $C_{(4)}$ (Ställberg-Stenhagen, Stenhagen, Sheppard, Sutherland, and Walsh, *Nature*, 1947, **160**, 580). From a comparison of its m. p. and *X*-ray spacings with those of synthetic hydrocarbons Ställberg-Stenhagen and Stenhagen (*J. Biol. Chem.*, 1948, **173**, 383; 1950, **183**, 223) concluded that phthiocerane is essentially racemic 4-methyltritriacontane, possibly containing small amounts of the optically active form, or of a higher homologue; they interpreted the formation of the racemic product as indicating that one of the functional groups of phthiocerol is attached at the carbon atom bearing the methyl group, or at an adjacent carbon atom.

In the present work phthiocerol, $[\alpha]_D$ −4·45°, m. p. 71·5—73°, was obtained from the lipids of human tubercle bacilli by a modification of the procedure described earlier (Chanley and Polgar, *J.*, 1954, 1003). Its infrared spectrum showed a band at 1712 cm.$^{-1}$ (CO), but purification of the product with the aid of Girard's T reagent indicated that ketonic material was only present as a minor contaminant. It has been claimed (Demarteau-Ginsburg, Ginsburg, and Lederer, *Biochim. Biophys. Acta*, 1953, **12**, 587) that phthiocerol, isolated by the procedure described by Anderson and his collaborators (*loc. cit.*, 1936), is accompanied by two ketones and a triol. Examination of our specimen by chromatography on alumina indicated that, if any triol was present, it could have been only a very small amount.

As already briefly reported (Hall and Polgar, *Chem. and Ind.*, 1954, 1293), phthiocerol was found to yield a benzylidene derivative, thus indicating the presence of a 1 : 2- or 1 : 3-glycol system; moreover, it afforded on oxidative degradation a liquid methoxy-acid, $C_{11}H_{22}O_3$, characterised through its *S*-benzylthiuronium salt, m. p. 137—139°, together with an acid, m. p. 76—77°, having the composition $C_{24}H_{48}O_2$ or a near homologue. We are grateful to Mrs. D. M. Hodgkin, F.R.S., for comparing the *X*-ray powder photograph of the latter acid with those of authentic specimens of *n*-tricosanoic and *n*-tetracosanoic acid (kindly provided by Dr. J. C. Smith). Mrs. Hodgkin reported as follows:

"The powder photographs of tetracosanoic acid and the degradation product seem to be essentially identical. They both show powder lines at the spacings 3·8, 4·1, 4·6, 11, 20, and 35 Å, but several of these lines seem to differ slightly in intensities. The powder photograph of tricosanoic acid shows powder lines at spacings of 3·8, 4·1, 4·7, 12, and 20 Å, but no line appears at 35 Å, while two additional lines appear at 3·7 and 18 Å."

On the assumption that the C_{11} methoxy-acid is a homogeneous substance, the above results show that phthiocerol has the structure (I) or (II) of which only (I) is compatible with the C_{34} formula proposed for the parent hydrocarbon (see above). In attempting to distinguish between these alternatives by examining the action of periodic acid on phthiocerol we found that a slow oxidation had taken place, and the product showed in its infrared spectrum a strong band at 1712 cm.$^{-1}$ (CO). In the earlier phases of this work (cf. Hall and Polgar, *loc. cit.*) we were, therefore, in favour of formula (I), but this view had to be revised in the light of the following evidence.

(I) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH(OH) \cdot C_9H_{18}(OMe)$

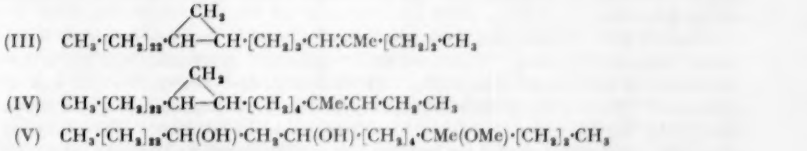
(II) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot C_9H_{18}(OMe)$

Reaction of phthiocerol with hydrogen bromide in glacial acetic acid at room temperature gave essentially a dibromide which, by the action of zinc and sodium iodide in acetone, afforded a bromine-free product. The latter, on oxidation with potassium permanganate in acetone, was found to contain only traces of olefinic material, probably formed by partial elimination of the methoxyl group. Since on debromination of a 1 : 2-dibromide an olefin should arise, these experiments indicated that phthiocerol is not a 1 : 2-diol, and the above bromine-free product must be largely a *cyclo*propane derivative resulting from the 1 : 3-diol (II) *via* the corresponding 1 : 3-dibromide. It should be noted that the infra-red spectrum of the dibromide showed, in addition to a weak band at 961·5 cm.$^{-1}$ (*trans*-CH : CH-), a moderate band at 1739 cm.$^{-1}$ (ester-carbonyl), probably due to the presence of a diacetoxy-derivative, a certain quantity of which may be expected to arise by the action of hydrogen bromide in acetic acid (cf. Stoll and Commarmont, *Helv. Chim. Acta*, 1948, **31**, 1077); however, judged from the analytical data for the debrominated material, the diacetoxy-derivative must have been a minor by-product.

A further proof for the 1 : 3-diol structure of phthiocerol was obtained by oxidation with a very dilute anhydrous solution of chromium trioxide in glacial acetic acid. The product, as shown by its ultraviolet and infrared spectra and a positive ferric chloride test (see Experimental section), consisted of a β-diketone and an αβ-unsaturated ketone, together with unchanged phthiocerol, and acidic oxidation products. A complete separation of the latter from the non-acid constituents was found in earlier experiments to involve considerable difficulties, and it should be pointed out that only traces of β-diketone resulted if water was added on dissolving the chromium trioxide in acetic acid.*

If the structure (II), representing phthiocerol as $C_{36}H_{74}O_3$, is accepted, it follows that the parent hydrocarbon must be $C_{35}H_{72}$. This conclusion conflicts with the view of Ställberg-Stenhagen and Stenhagen regarding the formula of phthiocerane (see above), but taking into account the 1 : 3-diol structure of phthiocerol it appears possible that in the procedure employed for transforming the latter into phthiocerane side-reactions may have occurred resulting in a mixture of isomers. Thus, the intermediate iodo-derivative, being a 1 : 3-di-iodide, may have given rise, by the action of zinc, to a *cyclo*propane derivative as a by-product; conversion of the latter into methyl-branched isomers could then have occurred during the subsequent catalytic hydrogenation. We believe, therefore, that the C_{36} formula for phthiocerol is not ruled out by the experimental evidence, namely, the *X*-ray and thermal data, recorded for phthiocerane (the infrared spectra did not differentiate between 4-methyltritriacontane and 4-methyltetratriacontane), but a final decision on this point must await the identification of the C_{11} oxidation product described above.

In further experiments phthiocerol was refluxed with a solution of hydrogen bromide in glacial acetic acid, and the resulting bromo-derivative debrominated with zinc and sodium iodide in acetone, to give an unsaturated hydrocarbon which gave correct analyses for $C_{35}H_{68}$ (when hydriodic acid was used instead of hydrogen bromide in glacial acetic acid, de-iodination of the product with zinc resulted in a hydrocarbon containing only a small proportion of unsaturated material.) Ozonisation of the unsaturated hydrocarbon afforded, in addition to non-volatile material presumed to be essentially a C_{30} acid and a C_{32} ketone, volatile products which were isolated as their 2 : 4-dinitrophenylhydrazones. Paper chromatography, kindly carried out by Dr. H. S. Burton, indicated the presence of the 2 : 4-dinitrophenylhydrazones of propaldehyde and methyl propyl ketone. These results suggested that the above unsaturated hydrocarbon was probably a mixture of the isomers (III) and (IV). It then follows that in phthiocerol presumably both the methoxyl and a methyl group are attached at $C_{(4)}$ as in (V). This conclusion is consistent with the earlier view (see above) that phthiocerane is essentially a racemic 4-methyl-substituted hydrocarbon.



(III) $CH_3 \cdot [CH_2]_{22} \cdot CH(CH_2) \cdot CH \cdot [CH_2]_2 \cdot CH{:}CMe \cdot [CH_2]_2 \cdot CH_3$

(IV) $CH_3 \cdot [CH_2]_{22} \cdot CH(CH_2) \cdot CH \cdot [CH_2]_4 \cdot CMe{:}CH \cdot CH_2 \cdot CH_3$

(V) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot [CH_2]_4 \cdot CMe(OMe) \cdot [CH_2]_2 \cdot CH_3$

Demarteau-Ginsburg and Lederer (*Compt. rend.*, 1955, **240**, 815) recently suggested that the methoxyl group is at $C_{(5)}$, and proposed formula (VI) for phthiocerol. This is incompatible with the results of our ozonisation experiments, since neither propaldehyde

(VI) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot [CH_2]_2 \cdot CH(OMe) \cdot CHMe \cdot [CH_2]_2 \cdot CH_3$

nor a non-volatile ketone could have resulted from structure (VI) by the procedure described; moreover, it does not account for the formation of a C_{11} methoxy-acid on oxidation of phthiocerol.

* During the later stages of this work, after the appearance of our preliminary note, Dr. Frank H. Stodola kindly placed at our disposal some unpublished results of studies made twenty years ago in Professor R. J. Anderson's laboratory, which involved oxidation of phthiocerol with chromic acid, and, judging from the high consumption of chromic acid and the liberation of over a mol. of carbon dioxide in this process, he concluded that phthiocerol probably has a 1 : 3-diol structure.

Experimental

All spectra were determined by Dr. F. B. Strauss with the technical assistance of Mr. F. Hastings; ultraviolet spectra were determined for MeOH solutions.

Isolation of Phthiocerol.—The procedure described in an earlier communication (Chanley and Polgar, *loc. cit.*) was followed with the following modifications. The methanol-insoluble product (about 500 g.) resulting from the partial hydrolysis of the lipids of tubercle bacilli (human type), dissolved in benzene (2·5 l.), was refluxed with potassium hydroxide (200 g.) in methanol (1 l.) for 200 hr., and the hot solution then filtered. In contrast to the earlier procedures which omitted this filtration, no emulsions were encountered in the subsequent operations involving acidification (dilute hydrochloric acid), ether-extraction, and washing of the combined extracts with water. After evaporation of the dried ($MgSO_4$) benzene–ether extracts, the residue (460 g.) was dissolved in benzene (2 l.), and methanol (5 l.) was added with shaking. Next day the precipitate (" mycolic acid;" 270 g.) was removed by filtration and washed with a mixture of benzene (200 c.c.) and methanol (500 c.c.); the combined filtrate and washings were evaporated. The residual product (190 g.) was dissolved in benzene (750 c.c.), and a solution of barium hydroxide (90 g.) in hot methanol (1 l.) added with stirring; the mixture was heated to boiling, and then kept at room temperature. Next day the solution was decanted, filtered (to remove insoluble barium salts), and concentrated (to about 1 l.), and the residual solution was poured into dilute hydrochloric acid. The aqueous layer was extracted with ether, and the ethereal extract, together with the benzene layer, washed with dilute hydrochloric acid, water, and dried ($MgSO_4$). After removal of the solvents, the residue (92 g.) was dissolved in boiling light petroleum (b. p. 40—60°; 500 c.c.). When the solution was kept overnight, a solid separated which after recrystallisation from ethyl acetate gave phthiocerol (32·5 g.) as colourless plates, m. p. 71·5—73°, $[\alpha]_D$ −4·45° (*c*, 11·48 in $CHCl_3$) (Found: C, 77·6; H, 13·4. Calc. for $C_{36}H_{74}O_3$: C, 78·0; H, 13·4%); its acetate, prepared by refluxing phthiocerol with acetic anhydride, distilled at 270—280° (bath)/0·04 mm. (Found: C, 75·15; H, 12·2. Calc. for $C_{40}H_{78}O_5$: C, 75·2; H, 12·2%).

The above petroleum mother-liquors from which the crude phthiocerol separated were found, on chromatography over alumina, to contain, largely, acidic material. Some earlier specimens of phthiocerol might have been contaminated with such acids.

Purification of Phthiocerol by Treatment with Girard-T Reagent.—Phthiocerol (1·14 g.) was refluxed with ethanol (50 c.c.), glacial acetic acid (5 c.c.), and Girard-T reagent (3 g.) for 1 hr., and the mixture then kept at room temperature overnight. On working up in the known manner (addition to ice-cold aqueous potassium hydroxide, ether-extraction) a " ketone " fraction (0·11 g.) resulted, the infrared spectrum of which showed a band at 1712 $cm.^{-1}$ (CO); this was absent in case of the " non-ketone " fraction (1 g.). It should be noted that during the above ether extractions and on washing the ethereal extracts with water, emulsions resulted which separated partly on standing, but complete separations of the organic and aqueous phases could not be achieved.

When 5 g. of phthiocerol were used, the " ketone " fraction resulting from the above procedure amounted to 1 g. The combined " ketonic " fractions (1·11 g.), when subjected to a repetition of the Girard separation, yielded 0·56 g. of " ketone." This was chromatographed in benzene (50 c.c.) on neutral alumina (activity II on the scale of Brockmann and Schodder, *Ber.*, 1941, **74**, 73) (15 g.; 1·4 × 9·5 cm.) prepared in benzene. The following fractions were obtained: (i) 0·005 g. eluted by benzene, (ii) 0·11 g. eluted by benzene–ether (4 : 1), (iii) 0·113 g. eluted by benzene–ether (7 : 3), (iv) 0·071 g. eluted by benzene–ether (3 : 2), (v) 0·081 g. eluted by ether, and (vi) 0·112 g. eluted by ether–methanol (19 : 1). The fraction (vi), which showed the strongest band at 1712 $cm.^{-1}$, was refluxed with ethanol (10 c.c.), hydroxylamine hydrochloride (0·1 g.), and sodium acetate (0·1 g.) for 5 hr., and, after dilution with water, the product was isolated by ether-extraction. For analysis the crude product was dried *in vacuo* at 100° for 1 hr. (Found: N, 2·3, 2·0%).

The above " non-ketone " fraction was chromatographed in benzene–ether (1 : 1) on neutral alumina (activity II), and the column eluted with the same solvent. Further elution with ether–methanol (19 : 1) removed small amounts of tenaciously held material which was rechromatographed under the same conditions, and the resulting ether–methanol eluate was subjected to a repetition of this procedure. The product finally eluted with ether–methanol had m. p. 70—75° after crystallisation from ethyl acetate and showed a medium band at 1093 $cm.^{-1}$ (aliphatic ether group); it represented about 0·6% of the original phthiocerol, and in view of the small amounts available was not investigated further.

Benzylidenephthiocerol.—A mixture of phthiocerol (0·2 g.), benzaldehyde (5 c.c.), and powdered anhydrous zinc chloride (1 g.) was shaken at room temperature for 12 hr. and set aside for a further 48 hr. Ether (50 c.c.) was then added and the solution shaken with anhydrous sodium carbonate (1 g.) for 1 hr. After filtration, the ethereal solution was washed successively with 5% aqueous sodium carbonate and water, then dried (Na_2SO_4) and evaporated. Trituration of the residue with methanol, followed by crystallisation of the separated solid from methanol, gave O-*benzylidenephthiocerol* as a colourless solid, m. p. 34—38° (Found: C, 80·4; H, 12·5. $C_{43}H_{78}O_3$ requires C, 80·4; H, 12·2%).

Oxidation of Phthiocerol with Periodic Acid.—Phthiocerol (1 g.) was dissolved in dioxan (100 c.c.), and a solution of periodic acid (1 g.) in water (5 c.c.) added; the resulting solution was kept at room temperature for about 3 weeks, then evaporated under reduced pressure at <30°, and the residue, after addition of water, isolated by ether-extraction. The product, which showed a strong band at 1712 cm.$^{-1}$ (CO) in its infrared spectrum, was chromatographed in benzene on alumina (activity I—II; 30 g.). Two main fractions were obtained, *viz.*, (i) a colourless solid (0·31 g.) eluted by benzene, and (ii) unchanged starting material, m. p. 72—73° (from acetone), eluted by ether–methanol. Fraction (i), after crystallisation from methanol, had m. p. 46—49° (sintering at *ca.* 43°) (Found: C, 80·2; H, 13·1%); an attempt was made to convert the crude material into a semicarbazone, but the product was shown on analysis to contain only a small amount of nitrogen (Found: N, 3·2%). Oxidation with a suspension of silver oxide in ethanolic sodium hydroxide gave small amounts of an acid which was not examined further.

Oxidation of Phthiocerol with Chromic Acid.—A solution of chromic acid (from 1 g. of chromium trioxide, 1 c.c. of water, and 10 c.c. of glacial acetic acid) was added dropwise to phthiocerol (0·5 g.) in glacial acetic acid (50 c.c.), kept at 25—30°, until no more chromic acid was consumed. After 1 hr. at the room temperature the mixture was poured into water, and the product isolated by ether-extraction. The crude material, combined with another batch which was obtained by a similar procedure (together 2 g.), was heated with glacial acetic acid (35 c.c.) and hydrogen peroxide (3 c.c.; 30%) on a steam-bath for 6 hr., a further portion of hydrogen peroxide (3 c.c.) being added after 3 hours' heating. Most of the acetic acid was then removed under reduced pressure, and the residue diluted with water and extracted with ether, from which the acidic fraction was removed by shaking with 2% aqueous potassium hydroxide (3 × 750 c.c.). Acidification of the alkaline extracts with hydrochloric acid, followed by ether-extraction and distillation, gave two acid fractions, *viz.*, (i) b. p. about 160° (bath)/40 mm., and (ii) b. p. 140° (bath)/0·1 mm. Fraction (i) (Found: C, 65·5; H, 10·7. Calc. for $C_{11}H_{22}O_3$: C, 65·3; H, 11·0%) afforded a *S*-benzylthiuronium salt which crystallised from aqueous ethanol as colourless plates, m. p. 137—139° (Found: C, 62·2; H, 8·6; N, 7·4; S, 8·2. Calc. for $C_{19}H_{32}O_3N_2S$: C, 62·0; H, 8·7; N, 7·6; S, 8·7%); OMe estimation of the acid gave erratic values (Found: OMe, 18·4, 12·8. Calc. for $C_{11}H_{22}O_3$: OMe, 15·35%). Fraction (ii), after crystallisation from acetone, had m. p. 76—77° (Found: C, 77·8; H, 12·8. Calc. for $C_{24}H_{48}O_2$: C, 78·2; H, 13·1%) (Ashton, Robinson, and Smith, *J.*, 1936, 283, give m. p. 84° for tetracosanoic acid). Its *amide*, after crystallisation from ethanol, had m. p. 112—113° (Found: C, 77·9; H, 13·3. $C_{24}H_{49}ON$ requires C, 78·4; H, 13·4%). The *p*-bromophenacyl ester, after crystallisation from ethanol, had m. p. 88—89° (Found: C, 67·5; H, 9·5. Calc. for $C_{32}H_{53}O_3Br$: C, 68·0; H, 9·4%) (Hann, Reid, and Jamieson, *J. Amer. Chem. Soc.*, 1930, **52**, 818, give m. p. 90—91° for the *p*-bromophenacyl ester of tetracosanoic acid). Examination of the infrared absorption of the acid and its amide (Nujol mulls) in the region 1350—1180 cm.$^{-1}$ (cf. Jones, McKay, and Sinclair, *J. Amer. Chem. Soc.*, 1952, **74**, 2575) indicated that the acid is tetracosanoic acid, and this was confirmed by the *X*-ray studies already described. The same acid was obtained by oxidation of phthiocerol with potassium permanganate in acetone, and also by drastic oxidation with chromic acid.

Mild Oxidation of Phthiocerol with Chromium Trioxide.—To a solution of phthiocerol (0·27 g., 0·0005 mole) in glacial acetic acid (150 c.c.) was slowly added a solution of chromium trioxide (0·066 g., 0·00066 mole) in glacial acetic acid (100 c.c.) at room temperature during 1 hr. The mixture was kept for 4 hr., then poured into water and extracted with ether. The extract was washed successively with aqueous sodium hydroxide and water, dried ($MgSO_4$), and evaporated. Ultraviolet light absorption of the crude product: max. 2200 and 2700 Å; ε 2700 and 2000, respectively. The infrared spectrum (film) indicated the presence of β-diketone (1610 and 1563 cm.$^{-1}$), free hydroxyl (3333 cm.$^{-1}$), and carboxyl groups (1706 cm.$^{-1}$). A solution of the product in ethanol–ether gave an immediate red colour on addition of anhydrous ferric chloride.

Conversion of Phthiocerol into a Dibromo-derivative.—Phthiocerol (2 g.) was kept with a solution of hydrogen bromide in glacial acetic acid (50% w/v; 25 c.c.) in a stoppered bottle at

the room temperature for 7 days. The mixture was then poured into water and extracted with ether. After being washed several times with water and dried ($MgSO_4$), the ethereal extract was evaporated, leaving a yellowish wax (Found: Br, 24·15. Calc. for $C_{36}H_{72}OBr_2$: Br, 23·5%).

Debromination of the Preceding Dibromide.—The dibromide (3·6 g.) was refluxed with dry acetone (100 c.c.), sodium iodide (10 g.), and zinc dust (6 g.) for 3 hr. The zinc dust was filtered off from the hot mixture and extracted with boiling chloroform (2 × 25 c.c.). The combined filtrates were poured into water and the whole was extracted with ether; the extract was washed with water, dried ($MgSO_4$), and evaporated. Distillation gave a bromine-free product, b. p. 255—265° (bath)/0·1 mm. (Found: C, 83·3; H, 13·8; no Br. Calc. for $C_{36}H_{72}O$: C, 83·1; H, 13·8%).

A portion (0·46 g.) of this product was refluxed with dry acetone (50 c.c.; previously distilled over $KMnO_4$) and potassium permanganate (0·5 g.) for 1 hr.; only 0·04 g. of acid was obtained; the bulk (0·38 g.) of the product appeared to be neutral.

Demethylation of Phthiocerol by the Action of Hydrogen Bromide and Debromination of the Product.—Phthiocerol (1·85 g.) was refluxed with a 50% w/v solution of hydrogen bromide in glacial acetic acid (20 c.c.) for 24 hr., and the mixture worked up as above. The resulting material (Found: Br, 26·9%), on debromination with zinc and sodium iodide in acetone by the procedure described in the preceding section, gave an unsaturated hydrocarbon (1·1 g.), b. p. 180° (bath)/0·5 mm. (Found: C, 86·1; H, 13·6. Calc. for $C_{35}H_{68}$: C, 86·1; H, 13·9%), showing in its infrared spectrum a band at 961·5 cm.$^{-1}$.

Ozonisation of the above Unsaturated Hydrocarbon.—Ozonised oxygen was passed through a solution of the hydrocarbon (1·1 g.) in dry carbon tetrachloride (25 c.c.) for 40 min. After removal of the solvent under reduced pressure at 40° (bath), water (25 c.c.) was added, and the mixture heated gradually to 100° (bath). During this operation volatile products were passed in a current of nitrogen into a receiver containing a solution of 2 : 4-dinitrophenylhydrazine in aqueous hydrochloric acid. A small quantity of dinitrophenylhydrazone was precipitated; this was dissolved in a little chloroform, and the solution examined (by Dr. H. S. Burton) by paper-chromatography according to the general procedure previously described (Burton, *Chem. and Ind.*, 1954, 576). On chromatograms including reference substances, run on Whatman No. 1 paper pretreated with diethyl tartrate (7·5% in aqueous methanol) or 70% aqueous ethyl lactate, and developed with light petroleum (b. p. 60—80°) containing 1·75% of carbon tetrachloride, spots corresponding to authentic specimens of the 2 : 4-dinitrophenylhydrazones of propaldehyde and methyl propyl ketone were detected.

The non-volatile material remaining in the residual aqueous mixture was isolated by ether-extraction, and the product refluxed with acetone (70 c.c.) and potassium permanganate (2 g.) for 1 hr. The precipitated manganese dioxide was filtered off, and the filtrate worked up as usual, to give a product, b. p. 220° (bath)/0·09 mm., which contained no acidic material and exhibited in its infrared spectrum a band at 1715 cm.$^{-1}$ (CO) (Found: C, 83·4; H, 13·4. Calc. for $C_{32}H_{62}O$: C, 83·1; H, 13·4%). The above manganese dioxide precipitate, after being worked up as usual, gave an acid of m. p. 69—71° (from acetone) which afforded an amide, b. p. 245° (bath)/0·06 mm. (Found: N, 3·6. Calc. for $C_{30}H_{59}ON$: N, 3·1%).

Reaction of Phthiocerol with Hydriodic Acid and De-iodination of the Product.—Phthiocerol (1 g.) was refluxed in a stream of nitrogen with constant-boiling hydriodic acid (10 c.c.; freshly distilled over red phosphorus) and phenol (1 g.) for 15 hr. (cf. Ginger and Anderson, *loc. cit.*). The mixture was cooled, poured into water, and distilled in steam to remove phenol. The residue was extracted with ether, and the ethereal solution washed with water, dried ($MgSO_4$), and evaporated. A pale-yellow wax (1·1 g.) was obtained which darkened in air (Found: I, 35·0. Calc. for $C_{35}H_{69}I_3$: I, 34·2; Calc. for $C_{35}H_{69}I_3$: I, 43·8%). This iodide (1 g.) was refluxed with acetone (80 c.c.) and zinc dust (5 g.) for 3 hr., and the mixture worked up as described above for a similar experiment involving the bromo-derivative. The product (0·42 g.) distilled at 200—220° (bath)/0·08 mm. (Found: C, 85·7; H, 14·0. Calc. for $C_{35}H_{70}$: C, 85·7; H, 14·3. Calc. for $C_{35}H_{68}$: C, 86·1; H, 13·9%). It showed a weak absorption band at 961·5 cm.$^{-1}$, and gave a low iodine value (15), indicating that a large proportion of the product had been reduced by the hydrogen iodide.

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Structural Aspects of the Hydrolysis of Titanium Tetraethoxide.

By D. C. Bradley, R. Gaze, and W. Wardlaw.

[Reprint Order No. 6280.]

The hydrolysis of titanium tetraethoxide in ethyl alcohol has been studied by an ebulliometric technique. The molecular complexities of the titanium oxide ethoxides produced by hydrolysis have been explained in terms of a structural theory based on the assumption that titanium exhibits the co-ordination number 6 in these compounds. The theory explains the unusual properties of titanium oxide ethoxides reported previously (*J.*, 1955, 721).

Recently (*J.*, 1955, 721) we reported that water reacted instantly with titanium tetraethoxide in dilute ethyl alcohol. The nature of the titanium oxide ethoxide produced depended on the initial molecular proportion of water to tetraethoxide and under certain conditions a crystalline compound (I) having an unexpected composition was isolated. In addition, we found that titanium oxide ethoxides were disproportionated by heat, and in the case of compound (I) there was no change in molecular complexity when disproportionation occurred in boiling ethyl alcohol. The hydrolysis of titanium tetraethoxide has now been further studied by an ebulliometric method.

Since no hydroxyl groups were detected in the products, the following " equation " may be used to represent the hydrolysis :

$$\mathrm{Ti{\cdot}OEt + H_2O + EtO{\cdot}Ti \longrightarrow Ti{\cdot}O{\cdot}Ti + 2EtOH}$$

This predicts an increase in molecular complexity as a result of hydrolysis and it seemed possible that a complete picture of the variation of molecular complexity with degree of hydrolysis might be obtained by conducting the hydrolysis in an ebulliometer. Water, in dilute alcoholic solution, was added in known quantities to the solution of the tetraethoxide in boiling alcohol and, from the changes in elevation of the boiling point, the apparent molecular complexity (n) (*i.e.*, the number of titanium atoms per " osmotic " molecule) was calculated. The results are presented in Fig. 1 in which the variation of complexity is plotted as a function of (h) [mol. ratio, H_2O : $Ti(OEt)_4$] for three different initial concentrations of titanium tetraethoxide.

Boyd (*J. Polymer Sci.*, 1951, **7**, 591) concluded from his studies on the hydrolysis of titanium alkoxides that linear polymers were probably formed in the region $h = 0$—1·0, as predicted for the reaction :

$$n\mathrm{Ti(OR)_4} + (n-1)\mathrm{H_2O} \longrightarrow \mathrm{(RO)_3Ti{\cdot}[O{\cdot}Ti(OR)_2]_{n-2}{\cdot}O{\cdot}Ti(OR)_3} + 2(n-1)\mathrm{ROH}$$

This leads to the simple relation :

$$n = 1/(1-h) \qquad \ldots\ldots\ldots \quad (1)$$

This has been plotted in Fig. 1 as curve D and a comparison with our experimental curves shows clearly that the hydrolysis of titanium tetraethoxide in boiling ethyl alcohol does not follow the requirements of Boyd's theory. It is implied in the derivation of equation (1) that the original titanium tetra-alkoxide is monomeric, although recent independent studies (Cullinane, Chard, Price, Millward, and Langlois, *J. Appl. Chem.*, 1951, **1**, 400; Caughlan, Smith, Katz, Hodgson, and Crowe, *J. Amer. Chem. Soc.*, 1951, **73**, 5652; Bradley, Mehrotra, Swanwick, and Wardlaw, *J.*, 1953, 2025) have demonstrated conclusively that many titanium tetra-alkoxides are polymeric. We suggest that, in the tetraethoxide and in all of the oxide ethoxides, titanium exhibits the co-ordination number 6 with respect to oxygen by virtue of intermolecular bonding. Further, we consider that the most probable structure for trimeric titanium tetraethoxide is that depicted in Fig. 2 (cf. Caughlan *et al.*, *loc. cit.*; ethyl groups omitted), whilst the oxide ethoxides are polymers built up by cross-linking of trimer units through Ti–O–Ti bridges. Although there are many ways in which this synthesis of polymers may be imagined to occur, there is one which appears to be unique and justifies exclusive consideration. This is illustrated by the section of polymer shown in Fig. 3 (some of the OEt groups are

omitted for clarity). The proposed structure, in which each titanium is quadrivalent but six-co-ordinate (distorted octahedra), can be extended indefinitely in one direction and corresponds to a series of compounds having the general formula $[Ti_{3(x+1)}O_{4x}(OEt)_{4(x+3)}]$, where $x = 0, 1, 2, 3 \ldots$, and the molecular complexity $(n) = 3(x + 1)$. It is on the basis of this structural model that we believe the nature of the hydrolysis of titanium tetraethoxide can best be interpreted. Thus when $x = 0$, the formula reduces to that of the trimeric tetraethoxide with the structure shown in Fig. 2. Moreover the first product of hydrolysis ($x = 1$) is, not $(EtO)_3Ti{\cdot}O{\cdot}Ti(OEt)_3$ as predicted by Boyd's theory, but is instead the compound $[Ti_6O_4(OEt)_{16}]$. Reference to Table 1 shows the composition of this compound in striking agreement with that found for the crystalline compound (I) (*loc. cit.*). The final column represents the " apparent " water content, determined on compound (I) by the Karl Fischer reagent and predicted for $[Ti_6O_4(OEt)_{16}]$ on the basis of our hypothesis

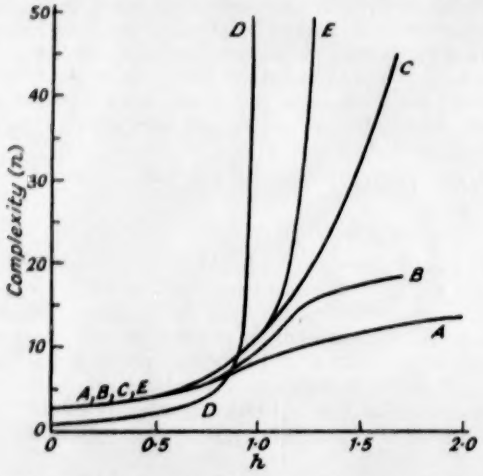


FIG. 1.
Initial concn. of $Ti_3(OEt)_{12}$:
A, 0·97%.
B, 4·31%.
C, 17·5%.

(*loc. cit.*) that oxygen exclusively linked to titanium should react with this reagent. Identifying compound (I) with $[Ti_6O_4(OEt)_{16}]$ and the structure illustrated in Fig. 4 (ethyl and some OEt groups omitted) it is clear that (I) was produced in the early stages of hydrolysis because it is the simplest hydrolysis product which may be formed. Further, addition of water to the tetraethoxide in the proportions $h = 0$—$0{\cdot}67$ should initially produce mixtures of $Ti_3(OEt)_{12}$ and compound (I), the amount of the latter rising to 100% at $h = 0{\cdot}67$. In the region $h = 0{\cdot}67$—$0{\cdot}89$ the theory predicts only mixtures of compound (I) and $[Ti_9O_8(OEt)_{20}]$, the amount of the former decreasing to zero at $h = 0{\cdot}89$. Therefore, starting from $h = 0$, the proportion of compound (I) produced should rise to a maximum at $h = 0{\cdot}67$ and decrease to zero as h approaches 0·89 and this accords with our previous observation (*loc. cit.*) that the maximum yield of crystalline compound corresponded to $h = 0{\cdot}5$.

TABLE 1.

	Ti (%)	EtO (%)	*M*	" H_2O " (%)
Compound (I)	26·1	67·7	1040 *	6·75
$Ti_6O_4(OEt)_{16}$	26·8	67·2	1072	6·71

* Cryoscopic determination in benzene.

Another product of hydrolysis which could be crystallised unchanged was compound (II), $TiO(OEt)_2$, and this corresponds to $[Ti_{12}O_{12}(OEt)_{24}]$ ($x = 3$). Its molecular weight (1730 in boiling benzene) is in reasonable agreement with the requirement of $[Ti_{12}O_{12}(OEt)_{24}]$ (1848).

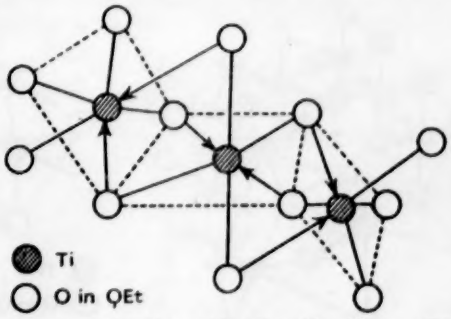
A further consequence of the theory is prediction of the ultimate linear polymer as an

infinitely long triple-chain molecule $[Ti_3O_4(OEt)_4]_\infty$ when $h = 1{\cdot}33$. This stage should mark the limit of soluble oxide-ethoxides because further hydrolysis must cause a fundamental change in structure leading to the production of insoluble giant molecules. It is noteworthy that precipitation occurred in the ebulliometric experiments in the region $h = 1{\cdot}5$—$2{\cdot}0$. In addition, it was previously observed that boiling an alcoholic solution of compound (II) containing sufficient water to give $h = 1{\cdot}75$ caused the precipitation of a substance (A). In another experiment, compound (I) was heated *in vacuo* at 200° until titanium tetraethoxide was no longer produced and a non-volatile residue (B) remained. Compound (II), when heated, similarly gave a non-volatile residue (C). Table 2 shows that (A), (B), and (C) are near in composition to the limiting formula $[Ti_3O_4(OEt)_4]$.

TABLE 2.

Compound	A	B	C	$Ti_3O_4(OEt)_4$
Ti (%)	39·1	35·7	37·5	37·0
OEt (%)	40·0	49·2	—	46·5

FIG. 2. $Ti_9(OEt)_{32}$.



A consideration of our general formula for the oxide ethoxides $[Ti_{3(x+1)}O_{4x}(OEt)_{4(x+3)}]$ shows that $n = 3(x + 1)$ and $h = 4x/3(x + 1)$, and elimination of x leads to the relation :

$$n = 12/(4 - 3h) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Therefore, a decisive test of the theory should be given by a comparison of the theoretical curve E based on the predictions of equation (2) and the experimental curves A, B, and C shown in Fig. 1. The agreement is reasonably good, particularly with curve C in the region $h = 0$—$1{\cdot}0$. A precise comparison in the region $h = 0$—$1{\cdot}33$ is shown in Table 3 in which n_1 and n_2 are values of n calculated from equations (1) and (2) and $n_{obs.}$ is the observed value of n from curve C. It is apparent that Boyd's theory is erroneous because

TABLE 3.

h	n_1	n_2	$n_{obs.}$	h	n_1	n_2	$n_{obs.}$	h	n_1	n_2	$n_{obs.}$
0	1·00	3·00	2·91	0·80	5·00	7·50	7·1	1·203	—	30·7	18·6
0·20	1·25	3·52	3·43	1·00	∞	12·0	11·7	1·297	—	110	21·9
0·40	1·67	4·29	4·12	1·02	—	12·7	12·2	1·333	—	∞	23·3
0·60	2·50	5·46	5·22	1·115	—	18·3	15·9				

it fails to consider the tendency of titanium to assume the co-ordination number **6** with oxygen although it might be applicable to the hydrolysis of a dialkoxydialkylsilane, *e.g.*, $Me_2Si(OEt)_2$, where the initial compound is monomeric and no cross-linking of polymer chains can occur.

Our theory also explains the surprising behaviour of compound (I) during disproportionation in solution. Thus it was previously found that the disproportionation in boiling alcohol did not cause any change in molecular complexity. However, this is in accord with the requirements of reactions (3) or (4) :

$$2[Ti_6O_4(OEt)_{16}] \longrightarrow [Ti_3(OEt)_{12}] + [Ti_9O_8(OEt)_{20}] \quad . \quad . \quad . \quad . \quad (3)$$

$$3[Ti_6O_4(OEt)_{16}] \longrightarrow 2[Ti_3(OEt)_{12}] + [Ti_{12}O_{12}(OEt)_{24}] \quad . \quad . \quad . \quad (4)$$

In fact, inspection of the general equation (5) ($y = 2, 3, 4 \ldots$) leads to the prediction that so long as the products of disproportionation of compound (I) conform to the structural model in Fig. 3 there will be no change in the average molecular complexity :

$$y[Ti_6O_4(OEt)_{16}] \longrightarrow (y-1)[Ti_3(OEt)_{12}] + [Ti_{3(y+1)}O_{4y}(OEt)_{4(y+3)}] \quad . \quad (5)$$

Moreover a similar behaviour is required for compound (II), or indeed for any member of the general series, as is shown by reaction (6) ($x = 1, 2, 3 \ldots$; $y = 2, 3, 4 \ldots$) :

$$y[Ti_{3(x+1)}O_{4x}(OEt)_{4(x+3)}] \longrightarrow (y-1)[Ti_3(OEt)_{12}] + [Ti_{3(xy+1)}O_{4xy}(OEt)_{4(xy+3)}] \quad . \quad (6)$$

Although we found experimentally that thermal disproportionation of compound (I) or (II) at 200° produced titanium tetraethoxide it might be argued against reactions (3), (4), (5), or (6) that the tetraethoxide may not be produced in boiling ethyl alcoholic solution.

FIG. 3. *Polymer*, $Ti_{3(x+1)}O_{4x}(OEt)_{4(x+3)}$.

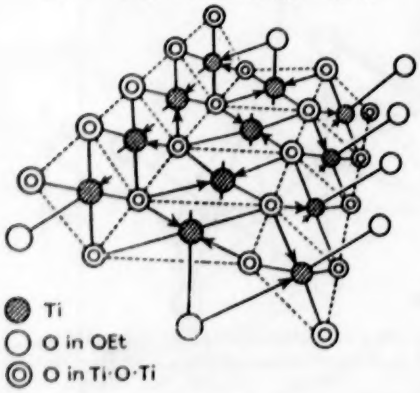
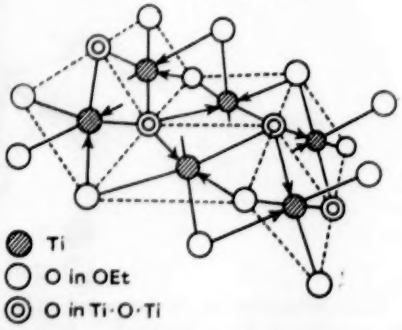


FIG. 4. $Ti_6O_4(OEt)_{16}$.



Nevertheless it is readily shown that disproportionation of any compound in our series will cause no change in average complexity provided that all the products conform to the same general series. A mathematical proof of this statement is as follows :

Let equation (7) represent the general process of disproportionation, *i.e.*,

$$r[Ti_{3(x+1)}O_{4x}(OEt)_{4(x+3)}] \longrightarrow s[Ti_{3(y/4+1)}O_y(OEt)_{(y+12)}] + t[Ti_{3(z/4+1)}O_z(OEt)_{(z+12)}] \quad . \quad (7)$$

Inspection shows that both products conform to the general formula of the starting material ($x = y/4 = z/4$). Consideration of the balance of titanium, oxygen, and ethoxide in (7) affords the relations :

$$3r(x+1) = 3s(y/4+1) + 3t(z/4+1) \quad . \quad . \quad . \quad . \quad . \quad . \quad (7a)$$

$$4rx = sy + tz \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7b)$$

$$4r(x+3) = s(y+12) + t(z+12) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7c)$$

Elimination of x, y, and z from equations (7*a*, *b*, and *c*) reveals that $r = s + t$; hence there is no change in average complexity during the reaction. Moreover by setting $y = 4x + q$ (*i.e.*, $y > 4x$) it follows that $z = 4x - sq/t$; thus if s and t are both finite and positive, then $4x > z$, showing that equation (7) represents a disproportionation. It is evident that our ebullioscopic investigation of the hydrolysis of titanium tetraethoxide only gave interpretable results because of this unique behaviour of the oxide ethoxides on disproportionation.

In view of the wide measure of agreement between theory and experiment it is important to consider possible explanations of certain discrepancies. For example,

curve *C* diverges from the theoretical for values of $h > 1{\cdot}1$ and, although the theoretical function is very sensitive to errors in h between 1·0 and 1·33 and the experimental error in determining n becomes high for the values $n > 10$, the magnitude of the divergence suggests that the theory does not apply under these conditions. Also it is noteworthy that the divergence becomes more marked at the lower initial concentrations of titanium tetraethoxide. It is reasonable to suppose that these discrepancies are connected with the fact that the complexity of the tetraethoxide itself is significantly less than 3 at the lower initial concentrations, and the theory hinges critically on the tetraethoxide's being trimeric. Although we found earlier that the tetraethoxide was trimeric in boiling benzene independently of concentration, it is not surprising that the complexity varies with concentration in alcohol because the donor property of this solvent should promote dissociation, *viz.* :

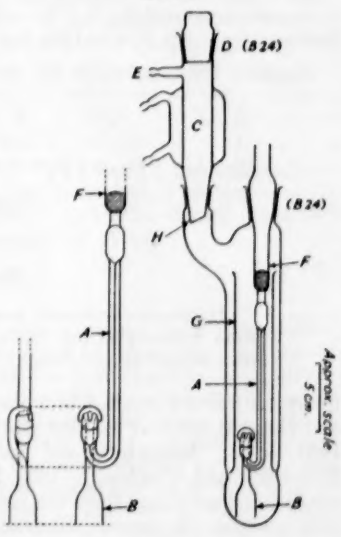
$$2[Ti_3(OEt)_{12}] + 6EtOH \rightleftharpoons 3[Ti_2(OEt)_8,2EtOH] \quad . \quad . \quad . \quad . \quad (8)$$

The same argument applies to the oxide ethoxides. For example, compound (I) with complexity 6·0 might be converted at a low concentration into an alcoholate (stable only in solution) of complexity 3·0 :

$$8EtOH + [Ti_6O_4(OEt)_{16}] \rightleftharpoons 2[Ti_3O_2(OEt)_8,4EtOH] \quad . \quad . \quad . \quad (9)$$

Hence it is quite feasible that at low concentrations of the ethoxide the complexity of the tetraethoxide and of the oxide ethoxides will be lower than that predicted by theory, as shown by curves *B* and *A*. Under our experimental conditions the molar concentration of oxide ethoxide declines as the extent of hydrolysis increases, and this should cause the lowering of complexity due to solvation to become correspondingly more marked. This tendency gives a qualitative explanation of the divergences noted for values of $h > 1{\cdot}0$. A detailed study of the reactions depicted in reactions (8) and (9) may provide the data necessary to derive a comprehensive relation between n, h, and the initial concentration of titanium tetraethoxide.

FIG. 5.



EXPERIMENTAL

Titanium tetraethoxide and dry ethyl alcohol were prepared by the methods previously described. The standard solution of water in alcohol was made up volumetrically, and was delivered to the ebulliometer from a microburette suitably protected from the atmosphere.

Ebulliometric Measurements.—An all-glass ebulliometer of special design (Fig. 5) was used with compounds which require special precautions to avoid hydrolysis. It was a modification of the Menzies–Wright ebulliometer (*J. Amer. Chem. Soc.*, 1921, **43**, 2309) and incorporated a differential water-thermometer (*A*) and a Cotrell lift pump (*B*). A wide-bore condenser (*C*) allowed rapid addition of solute through (*D*) without interruption of ebullition. The side-arm (*E*) was connected to a supply of dry nitrogen which prevented ingress of the atmosphere during the addition of solute. The nitrogen was pre-saturated with solvent to prevent loss from the ebulliometer. A mercury well (*F*) above the water-thermometer allowed the b. p. of the solvent in the ebulliometer to be determined to 0·1°. The water-thermometer was protected from cold condensate by a sealed-in glass jacket (*G*). A major source of error in the original Menzies–Wright apparatus was the uncertainty in the determination of the volume of boiling solvent. This has been overcome by a new method of calibrating the apparatus, which does not involve measuring the volume of solvent. Instead, the solvent (W_1 g.) in the ebulliometer

was weighed at room temperature with an error ~0·1%. The apparent ebullioscopic constant K_1 for 100 g. of solvent was then determined in the usual manner by noting the elevations of b. p. $\Delta T°$ c caused by successive additions of pure azobenzene. However, the rate of reflux of solvent was carefully noted by counting the drops of condensate falling from the drip-cone (H) of the condenser. The determination was then repeated with a different initial weight (W_2 g.) of solvent at the same reflux rate, and the new constant K_2 deduced. In this manner a calibration curve relating the ebullioscopic constant K_x with the initial weight of solvent (W_x g.) was constructed. Thence from the initial weight of solvent in any other experiment the appropriate value of K was deduced from the curve by interpolation. This method of calibration has a further advantage for experiments on the hydrolysis of titanium ethoxide where more solvent is added to the ebulliometer with each addition of water because of the ease with which the new value of K may be obtained.

In each experiment the following procedure was followed. First, the initial amount of solvent (W_1 g.) in the ebulliometer was determined and the "zero position" of the water thermometer found with boiling solvent. Then a known weight of titanium tetraethoxide was added and the elevation of the boiling point $\Delta T_1°$ was deduced from the new reading of the water-thermometer. From the values of ΔT_1, W_1, and K_1 the molecular complexity (n) of titanium tetraethoxide was deduced. A known quantity of standard aqueous ethyl alcohol was then added and the new elevation of the boiling point ΔT_2 was determined. The new weight of solvent W_1' was deduced from the equation $W_1' = (W_1 + x + y)$, where x g. was the weight of alcohol added as aqueous alcohol, and y g. was the weight of alcohol produced in hydrolysis from the known weight of water. From W_1' the new constant K_2 was evaluated. Thus the titanium oxide ethoxide of complexity n_1 caused the elevation ΔT_2 when dissolved in W_1' g. of alcohol and the theoretical elevation $\Delta T_2'$ for the same compound in W_1 g. of alcohol was determined from the expression: $\Delta T_2' = \Delta T_2(W_1'K_1)/(W_1K_2)$. The complexity of the oxide ethoxide was then deduced from the expression: $n_1 = n\Delta T_1/\Delta T_2'$. In practice these corrections were negligible in the early stages of hydrolysis and the simpler expression $n_1 = n\Delta T_1/\Delta T_2$ was used.

Each experimental curve in Fig. 1 is the result of over twenty determinations. Determinations were also made (for $h = 0$—1·3) with three other initial concentrations of ethoxide within the range 1—17·5% w/w and the shape of these curves resembled those presented in Fig. 1.

Birkbeck College, Malet St., London, W.C.1. [*Received, March 30th*, 1955.]

Xanthones. Part IV. A New Synthesis of Hydroxyxanthones and Hydroxybenzophenones.*

By P. K. Grover, G. D. Shah, and R. C. Shah.

[Reprint Order No. 6470.]

Hydroxy-xanthones and -benzophenones are conveniently obtained from hydroxybenzoic acids and phenols in presence of zinc chloride and phosphorus oxychloride.

Distillation of a mixture of a phenol, a phenolic acid, and acetic anhydride is the earliest and simplest method for the synthesis of hydroxyxanthones (Michael, *Amer. Chem. J.*, 1883, **5**, 81; Kostanecki and his co-workers, *Ber.*, 1891, **24**, 1896, 3981, etc.; Lund, Robertson, and Whalley, *J.*, 1953, 2438), but yields are often poor, experimental conditions are rather drastic, and there is a possibility of decarboxylation, autocondensation, and other side reactions (Lespegnol, Bertrand, and Dupas, *Bull. Soc. chim. France*, 1939, **6**, 1925; Lund *et al.*, *loc. cit.*). There are numerous other routes, but none is of general application and some require uncommon starting materials or involve a number of steps.

In continuation of the work on naturally occurring xanthones (*J. Indian Chem. Soc.*, 1953, **30**, 457, 463; *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 175; 1955, **14**, *B*, 153) the known methods for the synthesis of 1 : 3 : 7 : 8-tetrahydroxyxanthone or its tetramethyl ether

* Part III, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 175.

were found unsuitable. Condensation under mild conditions of a phenolcarboxylic acid with a reactive phenol in presence of condensing agents such as anhydrous aluminium chloride, phosphorus oxychloride, phosphoric oxide, or sulphuric acid was not promising; but a mixture of phosphorus oxychloride and fused zinc chloride, which had previously been found effective for the preparation of 2 : 4-dihydroxybenzophenone (Shah and Mehta, *J. Indian Chem. Soc.*, 1936, **13**, 368) gave highly satisfactory results, thus providing a new and convenient method for the synthesis of hydroxyxanthones (*Chem. and Ind.*, 1955, 62). In this method condensation of an *o*-hydroxybenzoic acid and a reactive phenol at about 60—80° for 1—2 hours, or in some cases even at room temperature, yields a hydroxyxanthone or a hydroxybenzophenone. The latter are best cyclised to xanthones by heating them alone at about 200—220° (Meyer and Conzetti, *Ber.*, 1897, **30**, 969) or with water in a sealed tube or in an autoclave at about 180—220° (Dutta and Watson, *J. Soc. Chem. Ind.*, 1911, **30**, 196), the latter method giving almost quantitative yields. It is interesting that oximation of 2 : 2′ : 4 : 4′-tetrahydroxybenzophenone gave the oxime of 3 : 6-dihydroxyxanthone, cyclisation having taken place simultaneously; however the oxime could not be hydrolysed to 3 : 6-dihydroxyxanthone.

The use of zinc chloride or phosphorus oxychloride alone is ineffective or much less efficient. Nenki's reaction, using fused zinc chloride alone, has been previously used for the preparation of some hydroxy-benzophenones and -xanthones, but the experimental conditions required are drastic and so the method is of limited use (Dutta and Watson, *J.*, 1912, **101**, 1238; Kostanecki, *Ber.*, 1894, **27**, 1989; Seshadri and Pankajmani, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 396).

A number of mono-, di-, and tri-hydroxybenzoic acids have been condensed with reactive phenols in typical syntheses by this method and ten xanthones and four benzophenones (some of them new) have been obtained. The following points are of interest: (1) Gentisic acid failed to condense, but its 5-monomethyl ether, did condense. (2) The method can be used when one or both the components is methylated. (3) Hydroxybenzoic acids condense in the β-position of the resorcinol nucleus as normally expected, whereas in Kostanecki's method condensations take place both in the β- and the γ-position, giving a mixture of 3 : 6- and 3 : 8-dihydroxyxanthones (Graebe, *Annalen*, 1889, **254**, 302; Bistrzycki and Kostanecki, *Ber.*, 1885, **18**, 1987). Orcinol condenses in the γ-position (cf. Shah and Saraiya, *Proc. Indian Acad. Sci.*, 1950, **31**, *A*, 213). (4) Xanthones are obtained directly when the acid component is a 2 : 6-dihydroxybenzoic acid, such as γ-resorcylic acid or phloroglucinolcarboxylic acid, or when the phenol is phloroglucinol or orcinol; *i.e.*, when the intermediate is a 2 : 6-dihydroxybenzophenone, it instantaneously cyclises to xanthone and cannot be isolated. This and the cyclisation during oximation may have a stereochemical cause.

Experimental

General Procedure.—A mixture of an *o*-hydroxybenzoic acid, a phenol, fused zinc chloride, and pnosphorus oxychloride was heated on a water-bath for 1½—2 hr., then cooled and poured into ice-water. The product was filtered off, washed with sodium hydrogen carbonate solution, and water, dried, and crystallised from suitable solvent. Acetates were prepared by acetic anhydride–pyridine, and methyl ethers by methyl sulphate, potassium carbonate, and acetone.

1 : 3-*Dihydroxyxanthone.*—Salicylic acid (1 g.), phloroglucinol (1·4 g.), freshly fused zinc chloride (3 g.), and phosphorus oxychloride (7 c.c.) were heated at 60—70° for 2 hr. The product was sublimed at 2 mm. and crystallised from dilute alcohol in needles, m. p. 256—258° (0·8 g.) (Robinson and Nishikawa, *J.*, 1922, **121**, 839, give m. p. 256—258°). The dimethyl ether crystallised as needles, m. p. 169—170°, from alcohol (Rao and Seshadri, *Proc. Indian Acad. Sci.*, 1953, **37**, *A*, 710, give m. p. 167—169°), and the diacetate, crystallised from alcohol, had m. p. 149° (*idem, ibid.*, give m. p. 145°) (Found: C, 65·3; H, 3·8. Calc. for $C_{17}H_{12}O_6$: C, 65·4; H, 3·9%).

2 : 2′ : 3 : 4-*Tetrahydroxybenzophenone.*—Salicylic acid (1 g.), pyrogallol (1·4 g.), zinc chloride (3 g.), and phosphorus oxychloride (7 c.c.) at 60—70° (2 hr.) gave the benzophenone, plates (from water), m. p. 103—104° which rose to 149° after drying at 100° in a vacuum (yield, 0·9 g.). This gave a blackish-green ferric reaction (Graebe and Eichengrün, *Annalen*, 1892,

269, 307, gave m. p. 102° with $1H_2O$) (Found : C, 63·4; H, 4·2. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1%). The *tetra-acetate*, crystallised from alcohol, had m. p. 117—118° (Found : C, 61·0; H, 4·6. $C_{21}H_{18}O_9$ requires C, 60·9; H, 4·3%).

3 : 4-*Dihydroxyxanthone.*—The foregoing benzophenone (0·5 g.) and water (20 c.c.) were heated under pressure at 180—200° for 5 hr. The solid xanthone produced crystallised from dilute alcohol as yellow plates, m. p. 240—241° (Graebe and Ullmann, *Ber.*, 1896, **29**, 824, give m. p. 240—241°). The dimethyl ether crystallised from alcohol in needles, m. p. 157° (Ullmann and Dinzler, *Ber.*, 1906, **39**, 433, give m. p. 156—158°). The diacetate (from alcohol) had m. p. 163—164° (Rao and Seshadri, *loc. cit.*, give m. p. 161—162°).

2 : 2′ : 4 : 4′-*Tetrahydroxybenzophenone.*—β-Resorcylic acid (5 g.), resorcinol (5 g.), freshly fused zinc chloride (20 g.), and phosphorus oxychoride (25 c.c.) were heated at 80—90° for 45 min. or kept for 48 hr. at room temperature. The benzophenone crystallised from boiling water in needles, m. p. 196—198° (6 g.) (Found : C, 63·1; H, 4·2. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1%). Shoesmith and Haldane (*J.*, 1924, **125**, 113) give m. p. 196—198°. The tetramethyl ether, crystallised from dilute alcohol, had m. p. 126—128° (Staudinger, Schlenker, and Goldstein, *Helv. Chim. Acta*, 1921, **4**, 341, give m. p. 129—130°), and the *tetra-acetate* (from alcohol), needles, had m. p. 146—147° (Found : C, 60·7; H, 4·25. $C_{21}H_{18}O_9$ requires C, 60·9; H, 4·4%).

3 : 6-*Dihydroxyxanthone Oxime from* 2 : 2′ : 4 : 4′-*Tetrahydroxybenzophenone.*—2 : 2′ : 4 : 4′-Tetrahydroxybenzophenone (0·4 g.) in a little alcohol and hydroxylamine hydrochloride (0·5 g.) in water (2 c.c.) and 10% sodium acetate solution (2 c.c.) were refluxed on a steam-bath for 1½ hr.; on cooling, 3 : 6-*dihydroxyxanthone oxime* separated. It crystallised from glacial acetic acid in plates, m. p. 283—285° (violet fluorescence in alkali) (Found : C, 63·8; H, 3·65; N, 6·1. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7; N, 5·8%).

3 : 6-*Dihydroxyxanthone.*—2 : 2′ : 4 : 4′-Tetrahydroxybenzophenone (0·5 g.) was heated in water (25 c.c.) at 200—220° (autoclave) for 2—2½ hr. On cooling, 3 : 6-dihydroxyxanthone was obtained in clusters of long needles. It was filtered off, washed, and crystallised from dilute pyridine. It did not melt below 330° and gave no ferric reaction. Its alkaline solution showed an intense violet fluorescence (Found : C, 68·6; H, 3·4. Calc. for $C_{13}H_8O_4$: C, 68·4; H, 3·5%) (Meyer and Conzetti, *Ber.*, 1897, **30**, 971, give decomp. >330°). It gave a diacetate (from alcohol), m. p. 205—206° (Kehrman, *Annalen*, 1910, **372**, 348, gives m. p. 204°), and a *dimethyl ether*, m. p. 186—187° (from alcohol) (Found : C, 70·0; H, 4·3. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%).

2 : 2′-*Dihydroxy*-4 : 4′-*dimethoxybenzophenone.*—2-Hydroxy-4-methoxybenzoic acid (0·9 g.), resorcinol monomethyl ether (1·0 g.), zinc chloride (3 g.), and phosphorus oxychloride (7 c.c.) were heated at 70—75° for 2 hr. The *benzophenone* crystallised from benzene in needles, m. p. 139—140° (0·4 g.) (Found : C, 65·4; H, 5·0. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·15%). It gave a brown ferric reaction, and was cyclised to 3 : 6-dimethoxyxanthone in water at 180—200°; this, when crystallised from alcohol, had m. p. and mixed m. p. 186—187°.

2 : 4 : 2′ : 3′ : 4′-*Pentahydroxybenzophenone.*—2 : 3 : 4-Trihydroxybenzoic acid (0·5 g.), resorcinol (0·5 g.), zinc chloride (3 g.), and phosphorus oxychloride (7 c.c.), heated at 70—80° for 1½ hr., gave the benzophenone, needles (from aqueous alcohol), (0·5 g.), m. p. 187—188°. It gave a dark brown ferric reaction and the alkaline solution became brown in air. Atkinson and Heilbron (*J.*, 1926, 2691) report m. p. 187°.

β-Resorcylic acid (1 g.), pyrogallol (1 g.), zinc chloride (6 g.), and phosphorus oxychloride (15 c.c.) when heated at 70—80° for 1 hr. yielded the same product, m. p. and mixed m. p. 187—188°.

3 : 4 : 6-*Trihydroxyxanthone.*—2 : 4 : 2′ : 3′ : 4′-Pentahydroxybenzophenone (0·5 g.) in water at 200—220° (2½ hr.) gave the xanthone, needles (from dilute alcohol), m. p. >340° (0·35 g.) (Dutta and Watson, *loc. cit.*, give m. p. >285°). This gave a dark green ferric colour and dissolved in alkali to an orange solution. Its triacetate (from acetic acid) had m. p. 209—210° and its *trimethyl ether* (from alcohol) melted at 153—154° (Found : C, 66·9; H, 5·0. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9).

3 : 8-*Dihydroxyxanthone.*—γ-Resorcylic acid (0·5 g.), resorcinol (0·5 g.), zinc chloride (4 g.), and phosphorus oxychloride (7 c.c.) at 65—70° (1½ hr.) gave the xanthone which crystallised from dilute alcohol or dilute aqueous pyridine as needles, m. p. 246—247° (0·2 g.) (Graebe, *Annalen*, 1889, **254**, 302, gave m. p. 245—246°), giving a greyish-green ferric colour (Found : C, 68·3; H, 3·6. Calc. for $C_{13}H_8O_4$: C, 68·4; H, 3·5%). The diacetate formed needles, m. p. 155°, from dilute alcohol (Graebe, *loc. cit.*, gives m. p. 124—130°) (Found : C, 64·9; H, 3·6. Calc. for $C_{17}H_{12}O_6$: C, 65·4; H, 3·9%).

1 : 3 : 6-*Trihydroxyxanthone.*—A mixture of phloroglucinolcarboxylic acid (1 g.), resorcinol (1 g.), zinc chloride (6 g.), and phosphorus oxychloride (15 c.c.) was heated at 65—70° for 1½—2 hr. or kept at room temperature for 48 hr. The xanthone produced was very soluble in ethanol and crystallised from dilute alcohol. Sublimed in a high vacuum, it had m. p. 323—324° (decomp.) (Found : C, 64·0; H, 3·3. Calc. for $C_{13}H_8O_5$: C, 63·9; H, 3·3%). It gave a reddish-brown ferric colour. The triacetate, prepared by acetic anhydride and a few drops of pyridine at 130—140° for 2 hr., crystallised from alcohol in needles, m. p. 172—173° (Found : C, 61·4; H, 3·9. Calc. for $C_{19}H_{14}O_8$: C, 61·6; H, 3·8%), and the *trimethyl ether* from alcohol in needles, m. p. 155—156° (Found : C, 67·0; H, 4·8. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%).

β-Resorcylic acid (2·5 g.), phloroglucinol (2·5 g.), zinc chloride (10 g.), and phosphorus oxychloride (30 c.c.) at 65—70° (1½ hr.) yielded the same product, m. p. 323—324° (decomp.) (1·2 g.) (triacetate, m. p. and mixed m. p. 172—173°).

Lund, Robertson, and Whalley (*loc. cit.*) reported m. p. 332° (decomp.) (triacetate, m. p. 160°) and described it as almost insoluble in alcohol, acetone, benzene, dioxan, or ethyl acetate.

1 : 6-*Dihydroxy*-3-*methylxanthone.*—β-Resorcylic acid (1 g.), orcinol (1 g.), zinc chloride (3·5 g.), and phosphorus oxychloride (7 c.c.), heated at 70—75° for 2 hr., gave the *xanthone*, needles (from dilute pyridine), m. p. 326—327° (0·8 g.), which gave a dark green colour with ferric chloride and a greenish fluorescence in alcohol (Found : C, 69·4; H, 3·8. $C_{14}H_{10}O_4$ requires C, 69·4; H, 4·2%). Its *diacetate* crystallised from dilute acetic acid in needles, m. p. 161—162° (Found : C, 65·6; H, 4·3. $C_{18}H_{14}O_6$ requires C, 66·2; H, 4·3%).

1-*Hydroxy*-6-*methoxy*-3-*methylxanthone* was prepared by partially methylating the preceding xanthone with methyl sulphate (1·2 mol.), potassium carbonate, and acetone. When crystallised from alcohol, it had m. p. 155—156° and gave a green ferric reaction and a green fluorescence in alcohol (Found : C, 69·8; H, 4·6. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%).

p-Orsellinic acid (0·5 g.), resorcinol (0·5 g.), zinc chloride (3 g.), and phosphorus oxychloride (7 c.c.) at 75—80° (1½ hr.) gave the same xanthone, m. p. and mixed m. p. 326—327°.

1 : 3-*Dihydroxy*-7-*methoxyxanthone* (iso*Gentisin*).—2-Hydroxy-5-methoxybenzoic acid (2 g.), phloroglucinol (2·2 g.), zinc chloride (6 g.), and phosphorus oxychloride (16 c.c.) were heated at 70—75° for 2 hr. The red solid obtained was sublimed at 230—240°/1—2 mm. and the yellow solid so obtained, when crystallised from dilute alcohol, had m. p. 239—240° (0·9 g.) (Shinoda, *J.*, 1927, 1984, gave m. p. 241° (Found : C, 65·0; H, 3·65. Calc. for $C_{14}H_{10}O_5$: C, 65·1; H, 3·9%). Acetylation yielded 1 : 3-diacetoxy-7-methoxyxanthone which, crystallised from acetic acid, had m. p. 210—212° (*idem*, *loc. cit.*, gives m. p. 211—212°). Methylation yielded 1 : 3 : 7-trimethoxyxanthone which crystallised from dilute methanol in plates, m. p. 171—173° (Rao and Seshadri, *loc. cit.*, give m. p. 171—173°). Demethylation of 1 : 3-dihydroxy-7-methoxyxanthone with hydriodic acid and acetic anhydride yielded 1 : 3 : 7-trihydroxyxanthone (gentisein) which crystallised from dilute alcohol in needles, m. p. 316—318° (olive-brown ferric colour) (*idem*, *ibid.*, give m. p. 316—318°).

1-*Hydroxy*-7-*methoxy*-3-*methylxanthone.*—2-Hydroxy-5-methoxybenzoic acid (2 g.), orcinol (2·2 g.), zinc chloride (6 g.), and phosphorus oxychloride (16 c.c.) at 70—75° (2 hr.) gave the *xanthone*, needles (from dilute pyridine), m. p. 155—156° (0·8 g.) (Found : C, 70·4; H, 4·8. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%). The *acetate* crystallised from alcohol in needles, m. p. 157—158° (Found : C, 68·4; H, 4·7. $C_{17}H_{14}O_5$ requires C, 68·5; H, 4·7%). Demethylation of 1-hydroxy-7-methoxy-3-methylxanthone (0·25) with hydriodic acid (10 c.c.; *d* 1·7) in acetic anhydride (5 c.c.) at 115—120° for 1½ hr. gave 1 : 7-dihydroxy-3-methylxanthone, m. p. 251—252° (from dilute pyridine), which gave a dark green ferric reaction (Kostanecki, *Ber.*, 1894, **27**, 1989, records m. p. 252°).

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The Effect of Bond Structure on the Baker–Venkataraman Transformation of Acetylanisoyloxyindanes and Benzoyloxytetrahydroacetonaphthones.

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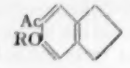
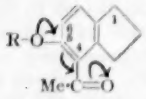
Further work on the Baker–Venkataraman transformation in the indane series is described (see Nowlan, Slavin, and Wheeler, *J.*, 1950, 340). A study of this reaction applied to *vic.*-benzoyloxytetrahydroacetonaphthones supports the view that the 1 : 2-bond in 5 : 6 : 7 : 8-tetrahydronaphthalene derivatives has a higher order than the 2 : 3-bond. The existence of steric strain in the acetyl group of 5 : 6 : 7 : 8-tetrahydro-2-hydroxy-1-acetonaphthone is demonstrated and its effects are discussed.

Nowlan, Slavin, and Wheeler (*J.*, 1950, 340) suggested on the basis of experiments with *vic.*-aroyloxyacetonaphthones that the Baker–Venkataraman transformation could be employed to study the bond structures of certain aromatic compounds. An advantage of using this reaction is that neither the aromatic bond nor the terminal carbon atoms of that bond are directly involved, as with other reactions (*e.g.*, Claisen rearrangement or ozonisation) used to study bond structure. Nowlan *et al.* (*loc. cit.*) showed that 5-acetyl-6-benzoyloxyindane (I*a*) rearranged to form the corresponding diketone, 5-benzoylacetyl-6-hydroxyindane more rapidly than 4-acetyl-5-benzoyloxyindane (II*a*) yields 4-benzoylacetyl-5-hydroxyindane. This result has now been confirmed by a study of 5-acetyl-6- and 4-acetyl-5-*p*-anisoyloxyindane (I*b* and II*b*); the transformation takes place more readily across the 5 : 6- than the 4 : 5-bond. These results suggest that the 5 : 6 bond in the indane derivatives studied is of a lower order than the 4 : 5-bond. The mobile π electrons in a double bond facilitate ester-type neutralisation of the carbonyl group in the

(I*a*; R = Bz)
(I*b*; R = *p*-MeO·C$_6$H$_4$·CO)
(I*c*; R = H)

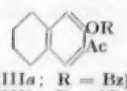




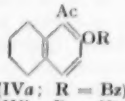
(II*a*; R = Bz)
(II*b*; R = *p*-MeO·C$_6$H$_4$·CO)
(II*c*; R = H)

acetyl radical. This hinders the Baker–Venkataraman transformation, which is to be regarded as a base-catalysed intramolecular condensation of the Claisen type (see II*a*, and Nowlan *et al.*, *loc. cit.*). The same conclusion with regard to bond order follows also from Wibaut and de Jong's ozonisation studies (*Bull. Soc. chim. France*, 1950, 996) and from Lothrop's results (*J. Amer. Chem. Soc.*, 1940, **62**, 132) on the Claisen rearrangement in indane compounds. It agrees, too, with the bond structure proposed for indane by Berthier and Pullman (*Bull. Soc. chim. France*, 1950, 88),* and is not contradicted by some recent infrared studies on indane derivatives by Hunsberger, Lednicer, Gutowsky, Bunker, and Taussig (*J. Amer. Chem. Soc.*, 1955, **77**, 2466).

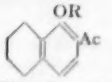
Transformation of Tetralin Derivatives.—The study has been extended to tetralin derivatives, and the transformations of 3-benzoyloxy-5 : 6 : 7 : 8-tetrahydro-2- (III*a*) and



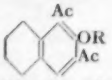
(III*a*; R = Bz)
(III*b*; R = H)
(III*c*; R = Ac)



(IV*a*; R = Bz)
(IV*b*; R = H)
(IV*c*; R = Me)



(V*a*; R = Bz)
(V*b*; R = H)



(VI*a*; R = Bz)
(VI*b*; R = H)

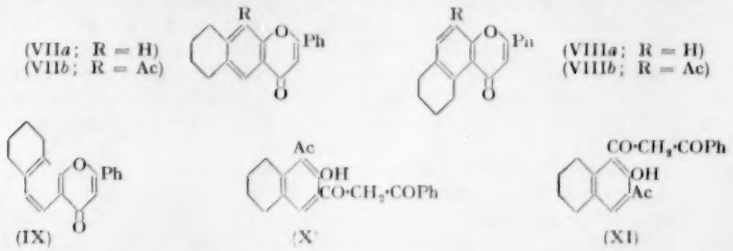
2-benzoyloxy-5 : 6 : 7 : 8-tetrahydro-1-acetonaphthone (IV*a*) and 1-benzoyloxy-5 : 6 : 7 : 8-tetrahydro-2-acetonaphthone (V*a*) into the corresponding diketones have been examined.

These diketones were cyclised to the respective flavone derivatives (VII*a*), (VIII*a*), and

* [Added, 1.10.55.] See also Horning and Amstutz, *J. Org. Chem.*, 1955, **20**, 1069.

(IX). The transformation of 1 : 3-diacetyl-2-benzoyloxy-5 : 6 : 7 : 8-tetrahydronaphthalene (VI*a*) gave two diketones, 4-acetyl-3-benzoylacetyl- (X) and 3-acetyl-1-benzoylacetyl-5 : 6 : 7 : 8-tetrahydro-2-naphthol (XI). These diketones were separated and cyclised to the corresponding flavone derivatives (VII*b*) and (VIII*b*) respectively, the structures of which are discussed below.

The rates of the transformations were in the order (VI*a* > III*a* > IV*a* > V*a*). The results with (III*a*), (IV*a*), and (V*a*) indicate that the order of the 1 : 2-bond is greater than that of the 2 : 3-bond, in agreement with Berthier and Pullman's theory (*loc. cit.*). However, the matter is complicated by stereochemical factors which now require discussion and which became apparent in the synthesis of the parent hydroxy-ketone of the ester (IV*a*).



Preparation of Hydroxy-ketones.—The hydroxy-ketones (III*b*), (IV*b*), and (VI*b*) are new. 5 : 6 : 7 : 8-Tetrahydro-3-hydroxy-2-acetonaphthone (III*b*) was obtained by Fries rearrangement of 5 : 6 : 7 : 8-tetrahydro-2-naphthyl acetate. The position of the acetyl group was confirmed by dehydrogenation of the product to 3-hydroxy-2-acetonaphthone; a new route to this not easily obtainable compound was thus provided (cf. Fries and Schimmelschmidt, *Ber.*, 1925, **58**, 2835; Virkar and Wheeler, *J.*, 1939, 1681).

1 : 3-Diacetyl-5 : 6 : 7 : 8-tetrahydro-2-naphthol (VI*b*) was prepared by Fries rearrangement of 3-acetoxy-5 : 6 : 7 : 8-tetrahydro-2-acetonaphthone (III*c*); it was separated from accompanying phenol (III*b*) by virtue of its insolubility in light petroleum. 5 : 6 : 7 : 8-Tetrahydro-2-hydroxy-1-acetonaphthone (IV*b*) was obtained from 1-bromo-5 : 6 : 7 : 8-tetrahydro-2-naphthyl methyl ether (Arnold, Zaugg, and Sprung, *J. Amer. Chem. Soc.*, 1941, **63**, 1314) which was converted into the Grignard compound, and thence, by treatment with acetonitrile, or with cadmium chloride followed by acetyl chloride, into 5 : 6 : 7 : 8-tetrahydro-2-methoxy-1-acetonaphthone (IV*c*), which was demethylated.

Demethylation of 5 : 6 : 7 : 8-*Tetrahydro-2-methoxy-1-acetonaphthone* (IV*c*).—This was investigated by three methods:

(*a*) A solution of the ether (IV*c*) in benzene was refluxed with aluminium chloride, and the phenol (IV*b*) was obtained. This was confirmed by remethylation to the initial methoxy-compound—the possibility of rearrangement (cf. Baddeley, *Quart. Rev.*, 1954, **8**, 355) was thus eliminated.

(*b*) A mixture of 5 : 6 : 7 : 8-tetrahydro-2-methoxy-1-acetonaphthone (IV*c*), aluminium chloride, and sodium chloride was heated at 170—190° (cf. Bruce, Sorrie, and Thomson, *J.*, 1953, 2403), and 5 : 6 : 7 : 8-tetrahydro-3-hydroxy-2-acetonaphthone (III*b*) was isolated. Demethylation was accompanied by a rearrangement which involved either a rearrangement of the reduced ring (Schroeter, *Ber.*, 1924, **57**, 1990) or an acyl-group migration (Baddeley, *J.*, 1944, 232).

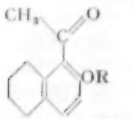
(*c*) A solution of the methoxy-ketone in a mixture of hydriodic acid and acetic anhydride, when kept at 45° for 48 hours (cf. Hutchins and Wheeler, *J.*, 1939, 91), formed 5 : 6 : 7 : 8-tetrahydro-2-naphthol. Demethylation was thus accompanied by an acid-catalysed deacylation (cf. Schubert and Latourette, *J. Amer. Chem. Soc.*, 1952, **74**, 1829).

The rearrangement reaction (method *b*) and the deacylation reaction (method *c*) suggest that the acetyl group in the phenol (IV*b*) is sterically hindered. Steric interference by the " alkyl " ring in tetralin with groups substituted in the positions *ortho* to the alkyl ring has previously been observed (see Van Helden, Verkade, and Wepster, *Rec. Trav. chim.*,

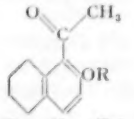
1954, **73**, 39; Fenton, DeWald, and Arnold, *J. Amer. Chem. Soc.*, 1955, **77**, 979). Accordingly, the ultraviolet spectra of the phenols (III*b*) and IV*b*) were examined for evidence of steric strain. The curve for the former corresponds closely with that for *o*-hydroxyacetophenone (Morton and Stubbs, *J.*, 1940, **1347**) when allowance is made for the bathochromic effect of the " alkyl " ring in (III*b*) (Jones, *Chem. Rev.*, 1943, **32**, 1). The peak in (III*b*) ($\lambda_{max.}$ 265 mμ, log ε 4·11) is largely suppressed in the isomer (IV*b*) ($\lambda_{max.}$ 255·5 mμ, log ε 3·35), presumably by steric inhibition of conjugation between the carbonyl group and the aromatic ring in the latter (cf. Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117). The second peak in the spectrum of (IV*b*) is at $\lambda_{max.}$ 296 mμ, log ε 3·31. This is probably due mainly to the hydroxyl group conjugated to the ring, for there is a peak in the curve of 5 : 6 : 7 : 8-tetrahydro-2-naphthol at $\lambda_{max.}$ 282·5 mμ, log ε 3·40, and Morton and Sawires (*J.*, 1940, 1052) report the maximum for phenol at $\lambda_{max.}$ 273 mμ, log ε 3·30. The peak at 296 mμ is broad, so in addition to the hydroxyl absorption there may be a contribution from the hindered conjugation of the carbonyl group with the aromatic ring. Such conjugation gives an absorption at $\lambda_{max.}$ 278 mμ, log ε 3·02 (Morton and Stubbs, *loc. cit.*). The bathochromic effect of the " alkyl " ring would shift this absorption into the region of the observed peak.

Discussion.—As stated above, the faster rearrangement of the ester (III*a*) than of its isomers (IV*a*) and (V*a*) is considered to be due to the low bond order of the 2 : 3-bond; this militates against ester-type neutralisation of the acetyl group and therefore promotes the Baker–Venkataraman transformation. In view of the strained nature of the acetyl group in (IV*b*) it is necessary to consider a possible steric effect in the transformation of (IV*a*). Examination of models of the Courtauld type (Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847) of the compounds (IV*a*) and (IV*b*) shows that the acetyl group in the 1-position is a hindered group in that the methyl group cannot pass across the reduced ring if the acetyl group is rotated about the bond joining it to the aromatic ring; on the other hand, there is no great hindrance as the carbonyl group is passed across the reduced ring. Thus it appears that of the two extreme positions for the acetyl group, (XII) and (XIII), the conformation (XIII) involves little strain and is favoured. This conclusion is similar to that of Kadesch (*J. Amer. Chem. Soc.*, 1944, **66**, 1207) for 2-methylacetophenone. The favoured orientation of the acetyl group in (XIII) is that required for the Baker–Venkataraman transformation, so that it would seem that the hindrance to rotation of the acetyl group can be ignored in considering the results of the Baker–Venkataraman reaction.

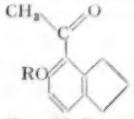
It has been shown that the steric effects of the trimethylene ring in indane are less than those of the tetramethylene ring in tetralin (Van Helden *et al.*, *loc. cit.*; Fenton, *et al.*, *loc. cit.*; Kooyman and Strang, *Rec. Trav. chim.*, 1953, **72**, 342). The study of models suggests that the orientation of the acetyl group in (II*a*), (II*b*), and (II*c*) is as in (XIV) rather than as in (XV). So in (II*a*) and (II*b*), as in (IV*a*), the steric hindrance of the acetyl group does does not affect the results of the Baker–Venkataraman transformation.



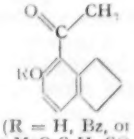
(R = H or Bz)
(XII)



(R = H or Bz)
(XIII)



(R = H, Bz, or
p-MeO·C$_6$H$_4$·CO)
(XIV)



(R = H, Bz, or
p-MeO·C$_6$H$_4$·CO
(XV)

With the Fries reaction, however, the hindered nature of the 1-position in 5 : 6 : 7 : 8-tetrahydronaphthalene derivatives, and of the 4-position in indanes, probably opposes the entrance of the acyl group migrating from the *ortho*-position. There is evidence that an intramolecular Fries migration to an *ortho*-position requires the formation of a bulky cyclic transition complex involving the ester grouping, aluminium chloride, and the *ortho*-carbon atom (Baltzly, Ide, and Phillips, *J. Amer. Chem. Soc.*, 1955, **77**, 2522). Hence, as indicated above, in the Fries rearrangement of 5 : 6 : 7 : 8-tetrahydro-2-naphthyl acetate, the migration is preferentially to the 3-position (cf. Sergievskaya and Morozovskaya,

J. Gen. Chem., U.S.S.R., 1945, **15**, 319; *Chem. Abs.*, 1946, **40**, 7187). Similarly, Baker (*J.*, 1937, 476) showed that acetyl migration in 5-acetoxyindane is preferentially to the 6-position. Thus with both the tetralin and the indane compounds the Fries migration is to the non-hindered position, although consideration of bond structure suggests that the alternative hindered position would be preferred. Baker's observation (*loc. cit.*) that 5-acetyl-6-hydroxyindane (I*c*) is more highly chelated than 4-acetyl-5-hydroxyindane (II*c*) may be related to steric resistance to conformation (XV).

One possibly anomalous result remains for mention. As stated above, the transformation of (VI*a*) leads to two diketones (X) and (XI) which were separated and then cyclised to the flavones (VII*b*) and (VIII*b*). The results of the transformations of (III*a*), (IV*a*), and (V*a*) suggest that the transformation of (VI*a*) should give (X) in greater yield than (XI). The recovery of purified (X) and (XI) from the crude transformation product was not quantitative, but in all experiments the yield of (XI) was greater than (X).

Structures of Acetyl-diketones and -flavones.—The structures of the acetyl-diketones and -flavones prepared were determined by deacylation of the acetylflavone (VII*b*) to give (VII*a*) by refluxing with 85% phosphoric acid (cf. Arnold and Rondestvedt, *J. Amer. Chem. Soc.*, 1946, **68**, 2176). This assignment of structures is supported by a study of the ultraviolet spectra of (VII*a*), (VII*b*), (VIII*a*), (VIII*b*), and (IX). The linear compounds (VII*a*) and (VII*b*) both show a peak at about 300 mμ, more intense than a second peak at 260 mμ. The curve of (VII*a*) differs from that of flavone (Davis and Geissman, *J. Amer. Chem. Soc.*, 1954, **76**, 3507) by the expected bathochromic shift caused by the "alkyl" ring. The peaks at about 300 mμ in the spectra of the angular-type compounds (VIII*a*) and (VIII*b*) are similar to each other and are less intense than second peaks at 260 mμ. Compound (IX) has also an angular structure but differs from (VIII*a*) and (VIII*b*) in that the point of fusion of one end of the alkyl ring is *ortho* to the position of fusion of the oxygen of the γ-pyrone ring. In the spectrum of (IX), the peak at 300 mμ is lower than that at 260 mμ but the difference in intensity is not as marked as that in the isomeric flavone (VIII*a*) or its acetyl derivative (VIII*b*).

It should be stressed that, although the transformation experiments support the Berthier–Pullman view of the bond structure of indane and tetralin, yet the results apply strictly only to the compounds studied.

Experimental

Ethanol was used for crystallisation and for absorption measurements unless otherwise stated.

Anisates of o-Hydroxyacetylindanes.—Preparation. 5-Acetyl-6- (I*c*) and 4-acetyl-5-hydroxyindane (II*c*) were prepared as described by Baker (*J.*, 1937, 476). *5-Acetyl-6-p-anisoyloxyindane* (I*b*), obtained from (I*c*) by the pyridine–acid chloride method and crystallised from ethanol or ligroin, had m. p. 128—129° (Found: C, 73·2; H, 5·7. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·9%). The isomeric *4-acetyl-5-p-anisoyloxyindane* (II*b*), m. p. 81—83° (aqueous ethanol or ligroin) (Found: C, 72·9; H, 5·9%), was prepared from (II*c*) in a similar manner.

Baker–Venkataraman transformation. A solution of the ester (I*b*) (0·5 g.) in pyridine (5 ml.) was shaken with potassium hydroxide (0·5 g.) which had previously been powdered in a hot mortar. The product was acidified, and the precipitate collected. *5-p-Anisoylacetyl-6-hydroxyindane* (0·3 g.) separated in yellow needles, m. p. 142—143° (Found: C, 73·2; H, 6·0. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·9%); the *4-p-anisoylacetyl-5-hydroxy-analogue* [from (II*b*)] formed orange crystals, m. p. 114—115° (Found: C, 73·3; H, 5·6%). When the transformations were carried out simultaneously under standard conditions, reaction with ester (I*b*) commenced immediately and was complete in 20 min., whereas ester (II*b*) did not react for 20 min. and complete separation of the salt of the diketone required several hours.

Preparation of 4′-Methoxycyclopentenoflavones.—A solution of the diketone from ester (I*b*) (0·2 g.) in glacial acetic acid (2 ml.) was boiled with a few drops of concentrated hydrochloric acid for 1 min. Hot water was added until an opalescence appeared, and the mixture was boiled again and cooled to separate *4′-methoxy-6*: 7-*cyclopentenoflavone*,* m. p. 198—199° (Found: C, 77·5; H, 5·6. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%). *4′-Methoxy-5*: *6-cyclopentenoflavone*,* obtained from (II*b*), had m. p. 176—177° (from aqueous acetic acid) (Found:

* In these compounds the primed numerals refer to positions in the phenyl group of flavone.

C, 77·3; H, 5·6%). These flavones in sulphuric acid showed a blue ultraviolet fluorescence. The first isomer was also prepared (mixed m. p.) by heating a solution of (I*b*) (0·2 g.) in distilled glycerol (2 ml.) for 30 min. at 250° in an atmosphere of nitrogen (cf. Lynch, O'Toole, and Wheeler, *J.*, 1952, 2063) and pouring the hot solution into water (20 ml.).

Preparation of Tetrahydrohydroxyacetonaphthones.—5 : 6 : 7 : 8-Tetrahydro-1-hydroxy-2-acetonaphthone (V*b*) was prepared by Sergievskaya and Morozovskaya's method (*J. Gen. Chem., U.S.S.R.*, 1944, **14**, 1107; *Chem. Abs.*, 1946, **40**, 7186).

5 : 6 : 7 : 8-*Tetrahydro-3-hydroxy-2-acetonaphthone* (III*b*). A mixture of 2-acetoxy-5 : 6 : 7 : 8-tetrahydronaphthalene (Schroeter, *Annalen*, 1922, **426**, 83) (116 g.) and aluminium chloride (116 g.) was heated at 120° for 1½ hr., and the product decomposed by ice and hydrochloric acid. The resulting 5 : 6 : 7 : 8-*tetrahydro-3-hydroxy-2-acetonaphthone* (III*b*) separated from ethanol or aqueous acetone in pale yellow needles (64 g.), m. p. 72—73°, which gave a violet ethanolic ferric colour (Found: C, 75·9; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%). For confirmation of structure a mixture of (III*b*) (2 g.) and 30% palladised charcoal (0·2 g.) was heated at 270—300° in carbon dioxide (2 hr.). Extraction with ether gave a solid which crystallised in yellow plates, m. p. 106—108°, raised to 111—113° by addition of 3-hydroxy-2-acetonaphthone (m. p. 112—113°).

1 : 3-*Diacetyl-5 : 6 : 7 : 8-tetrahydro-2-naphthol* (VI*b*). Acetylation of the acetonaphthone (III*b*) (25 g.) (sodium acetate–acetic anhydride) gave its 2-*acetate* (III*c*) which crystallised in colourless prisms (24·5 g.), m. p. 55—57° (Found: C, 72·1; H, 6·6. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). A mixture of this (7·5 g.) and aluminium chloride (7·5 g.) was kept at 75—80° for 6 hr. and the product was decomposed by ice and hydrochloric acid. The resulting black solid was washed with cold light petroleum (b. p. 40—60°). The residual 1 : 3-*diacetyl-5 : 6 : 7 : 8-tetrahydro-2-naphthol* (VI*b*) crystallised from ethanol (charcoal) or acetone in pale yellow rhombs (1·5 g.), m. p. 128—130°, which gave a purple ethanolic ferric colour (Found: C, 72·2; H, 6·8%).

5 : 6 : 7 : 8-*Tetrahydro-2-hydroxy-1-acetonaphthone* (IV*b*). 1-Bromo-5 : 6 : 7 : 8-tetrahydro-2-naphthol (Schroeter, *loc. cit.*) was methylated by potassium carbonate–methyl sulphate–acetone to form 1-bromo-5 : 6 : 7 : 8-tetrahydro-2-naphthyl methyl ether; Arnold, Zaugg, and Sprung's method (*loc. cit.*) was less satisfactory. Alternatively, 5 : 6 : 7 : 8-tetrahydro-2-naphthol was methylated as above (cf. Schroeter, *loc. cit.*) and treated with bromine in acetic acid to yield the bromo-methoxy-compound.

5 : 6 : 7 : 8-*Tetrahydro-2-methoxy-1-acetonaphthone* (IV*c*). (i) A solution of acetonitrile (5·5 ml.) in ether (25 ml.) was added dropwise during 20 min. to a stirred boiling Grignard solution from 1-bromo-5 : 6 : 7 : 8-tetrahydro-2-naphthyl methyl ether (32·7 g.), ether (170 ml.), magnesium (4·9 g.), iodine (trace), and ethyl bromide (trace) (cf. Arnold, Zaugg, and Sprung, *loc. cit.*). Stirring and refluxing were continued for 2 hr. Next day, the Grignard complex was decomposed by ice (300 ml.) and concentrated hydrochloric acid (200 ml.), the ether evaporated, and the acid solution refluxed for 2 hr. The ethereal solution of the resulting oil was washed with dilute aqueous sodium hydroxide and dried (Na_2SO_4). Evaporation of the solvent gave an oil; the fraction of this oil with b. p. 158—170°/8 mm. solidified. 5 : 6 : 7 : 8-*Tetrahydro-2-methoxy-1-acetonaphthone* (IV*c*) crystallised from light petroleum (b. p. 60—80°) or methanol in needles, m. p. 81—82° (2·2 g.) (Found: C, 76·4; H, 8·2. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%).

(ii) Cadmium chloride (5·4 g.) was added rapidly with stirring to a cooled Grignard solution from the bromo-ether (12 g.), ether (60 ml.), magnesium (1·6 g.), ethyl bromide (trace), and iodine (trace), and the mixture was refluxed for 2½ hr. More cadmium chloride (0·5 g.) was added, and the heating continued for 1½ hr. Gilman and Schulze's colour test (*J. Amer. Chem. Soc.*, 1925, **47**, 2002) was negative. Ether was then replaced by benzene and the final solution volume was adjusted to 50—60 ml. (cf. Cason, *J. Amer. Chem. Soc.*, 1946, **68**, 2078). Acetyl chloride (4 ml.) in benzene (60 ml.) was added dropwise to the stirred boiling cadmium aryl solution, and the mixture was refluxed for 8 hr. and poured on ice and dilute sulphuric acid. Removal of the solvent from the washed (dilute aqueous NaOH) and dried benzene solution afforded 5 : 6 : 7 : 8-tetrahydro-2-methoxy-1-acetonaphthone (IV*c*) (1·8 g.) (mixed m. p. confirmation with the product of the acetonitrile reaction).

Demethylation. (*a*) By aluminium chloride in benzene: a solution of (IV*c*) (1·3 g.) in benzene (130 ml.) was refluxed with aluminium chloride (13 g.) for 45 min. The solid formed was decomposed by ice and hydrochloric acid, followed by boiling of the mixture for 30 min. The product was collected in ether, extracted from the ethereal solution with dilute aqueous sodium hydroxide, and recovered by acidification. 5 : 6 : 7 : 8-*Tetrahydro-2-hydroxy-1-acetonaphthone* (IV*b*) crystallised from light petroleum (b. p. 40—60°) or methanol in needles, m. p. 112—113°

(Found : C, 75·2; H, 7·5. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%), which gave a faint green ethanolic ferric colour. Remethylation of the product (methyl sulphate–potassium carbonate–acetone) gave (IV*c*) (mixed m. p. confirmation).

(*b*) By aluminium chloride in fused sodium chloride (cf. Bruce, Sorrie, and Thomson, *J.*, 1953, 2403) : a mixture of (IV*c*) (0·5 g.), sodium chloride (0·5 g.), and aluminium chloride (2·5 g.), which had been heated at 170—190° for 3 min., was poured on ice and hydrochloric acid, and decomposition of the aluminium chloride complex was completed by heating the mixture on a steam-bath for 15 min. The product was collected in ether, the ethereal solution washed with dilute aqueous sodium hydroxide, and the hydroxide solution acidified. The precipitate of 5 : 6 : 7 : 8-tetrahydro-3-hydroxy-2-acetonaphthone (III*b*) was again collected in ether. It crystallised in pale yellow needles (0·012 g.), m. p. 68—69° alone or mixed with authentic (III*b*) (Found : C, 75·2; H, 7·6. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%).

(*c*) By hydriodic acid and acetic anhydride (cf. Hutchins and Wheeler, *J.*, 1939, 91) : a mixture of (IV*c*) (1·4 g.), acetic anhydride (12 ml.), and hydriodic acid (12 ml., 55%) was kept for 48 hr. at 45° and poured into saturated aqueous sodium hydrogen sulphite. 5 : 6 : 7 : 8-Tetrahydro-2-naphthol, isolated by ether-extraction, crystallised from light petroleum in rhombs (0·4 g.), m. p. and mixed m. p. 59—62° (Found : C, 80·6; H, 8·2. Calc. for $C_{10}H_{12}O$: C, 81·0; H, 8·2%).

Preparation of the benzoates of (III*b*), (IV*b*), (V*b*), and (VI*b*). The following benzoates (the first three are isomers) were prepared by using pyridine and benzoyl chloride : 1-*benzoyloxy*-5 : 6 : 7 : 8-*tetrahydro*-2-*acetonaphthone* (V*a*) separated in rhombs from methanol, ethanol, or light petroleum (b. p. 60—80°), m. p. 102—104° (Found : C, 77·4; H, 6·1. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·2%); 3-*benzoyloxy*-5 : 6 : 7 : 8-*tetrahydro*-2-*acetonaphthone* (III*a*) formed plates, m. p. 81—82°, from ethanol or aqueous acetone (Found : C, 77·0; H, 5·8%); 2-*benzoyloxy*-5 : 6 : 7 : 8-*tetrahydro*-1-*acetonaphthone* (IV*a*) crystallised in needles, m. p. 62—63° from ligroin or methanol (Found : C, 77·7; H, 6·6%); 1 : 3-*diacetyl*-2-*benzoyloxy*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (VI*a*) separated in rhombs, m. p. 116—117° (Found : C, 74·5; H, 5·8. $C_{21}H_{20}O_4$ requires C, 75·0; H, 6·0%).

Transformation of foregoing benzoates. The method of transformation was that used in transforming the *o*-acetylanisoyloxyindanes. The following products were isolated (the colours given with ethanolic ferric chloride are noted in parentheses) :

From (V*a*) : 2-*Benzoylacetyl*-5 : 6 : 7 : 8-*tetrahydro*-1-*naphthol* (0·28 g.), orange needles, m. p. 117—119° (green) (Found : C, 75·4; 75·6; H, 5·8, 6·0. $C_{19}H_{16}O_3.\frac{1}{2}H_2O$ requires C, 75·2; H, 6·3%).

From (III*a*) : 3-*Benzoylacetyl*-5 : 6 : 7 : 8-*tetrahydro*-2-*naphthol* (0·325 g.), yellow-orange needles, m. p. 107—108° (brown) (Found : C, 78·0; H, 6·3. $C_{19}H_{16}O_3$ requires C, 77·5; H, 6·2%).

From (IV*a*) : the crude product (0·41 g.) (red-brown) exhibited in sulphuric acid a green ultraviolet fluorescence. About 10% of it was insoluble in sodium hydroxide; this indicated that the reaction had yielded 1-benzoylacetyl-5 : 6 : 7 : 8-tetrahydro-2-naphthol and 5 : 6-*cyclo*hexenoflavone (VIII*a*). The crude diketone was directly cyclised to the flavone (see below).

From (VI*a*) : a mixture of 1-*acetyl*-3-*benzoylacetyl*- (X) (practically insoluble in cold ether) and 3-*acetyl*-1-*benzoylacetyl*-5 : 6 : 7 : 8-*tetrahydro*-2-*naphthol* (XI) (soluble in cold ether) was obtained. Compound (X) crystallised from acetone in orange rhombs, m. p. 166—168° (0·065 g.) (brown) (Found : C, 74·8; H, 5·8. $C_{21}H_{20}O_4$ requires C, 75·0; H, 6·0%). Compound (XI) (0·14 g.) was obtained in light yellow needles, m. p. 118—119° (red) (Found : C, 74·8; H, 5·7%).

When the four transformations were carried out under standard conditions the following results were obtained (yields of crude diketones are given in parentheses) :

Compound	Colour deepens in	Salt separates in	Reaction complete in	Yield (%)
(V*a*)	2—5 min.	25—35 min.	180—240 min.	80
(III*a*)	5 ,,	10—15 ,,	30—60 ,,	89
(IV*a*)	10—15 ,,	20 ,,	120—180 ,,	83
(VI*a*)	At once	5 ,,	15—60 ,,	90

The general conclusion is that the relative transformation rates were : (VI*a*) > (III*a*) > (IV*a*) > (V*a*).

Preparation of cyclo*Hexenoflavones.*—These were prepared by cyclising the corresponding diketones by the method described for the preparation of the 4′-methoxy*cyclo*pentenoflavones. The following flavones were thus prepared (the colours noted in parentheses are those of the fluorescence in concentrated sulphuric acid) :

7 : 8-cyclo*Hexenoflavone* (IX), needles, m. p. 194—195° (Found : C, 82·3; H, 5·8. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·8%) (blue-green). 6 : 7-cyclo*Hexenoflavone* (VII*a*), small needles, m. p. 170—171° (Found : C, 82·0; H, 5·8%) (blue). 5 : 6-cyclo*Hexenoflavone* (VIII*a*) [from cyclisation of crude product obtained by transformation of (IV*a*)], needles, m. p. 130—131° (Found : C, 82·9; H, 6·0%). The flavone was purified by vacuum-sublimation followed by crystallisation (green). 8-*Acetyl*-6 : 7-cyclo*hexenoflavone* (VII*b*), rhombs, m. p. 188—190° (Found : C, 79·4; H, 6·0. $C_{21}H_{18}O_3$ requires C, 79·2; H, 5·7%) (blue). 8-*Acetyl*-5 : 6-cyclo*hexenoflavone* (VIII*b*), pale yellow needles, m. p. 175—177° (Found : C, 78·7; H, 5·4%) (green). Cyclisation was not complete and it was necessary to remove uncyclised diketone by extraction with ether in which the flavone was almost insoluble. The flavone was purified by sublimation at 2 mm., followed by crystallisation.

Confirmation of Structures assigned to the Acetylflavones (cf. Arnold and Rondestvedt, *J. Amer. Chem. Soc.*, 1946, **68**, 2176). A solution of (VII*b*) (0·15 g.) in phosphoric acid (85%; 10 ml.) was refluxed for 5 hr. and poured into water. The resulting precipitate crystallised from ethanol (charcoal) in needles, m. p. 169—171°, alone or mixed with (VII*a*).

Table of maxima observed in ultraviolet spectra.

Compound	$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε
5 : 6 : 7 : 8-Tetrahydro-3-hydroxy-2-acetonaphthone (III*b*)	339·5	3·60	265·5	4·11	—	—
Product from demethylation of 5 : 6 : 7 : 8-tetrahydro-2-methoxy-1-acetonaphthone by use of $AlCl_3$–NaCl at 170—190° (III*b*)	340·5	3·58	264	4·10	—	—
5 : 6 : 7 : 8-Tetrahydro-2-hydroxy-1-acetonaphthone (IV*b*)	296	3·31	255·5	3·35	—	—
5 : 6 : 7 : 8-Tetrahydro-2-naphthol	331	2·36	282·5	3·40	225	4·11
6 : 7-*cyclo*Hexenoflavone (VII*a*)	304	4·41	260·5	4·39	—	—
8-Acetyl-6 : 7-*cyclo*hexenoflavone (VII*b*)	302	4·41	260·0	4·30	—	—
5 : 6-*cyclo*Hexenoflavone (VIII*a*)	297	4·56	255·5	4·45	—	—
8-Acetyl-5 : 6-*cyclo*hexenoflavone (VIII*b*)	300	4·23	258·5	4·30	220	4·50
7 : 8-*cyclo*Hexenoflavone (IX)	300·5	4·30	260·5	4·35	—	—

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Triterpenoids. Part XLV. The Conversion of α-Amyrin into Phyllanthol. The Constitution of "iso-α-Amyradienonyl-II Acetate."*

By J. M. BEATON, J. D. EASTON, M. M. MACARTHUR, F. S. SPRING, and ROBERT STEVENSON.

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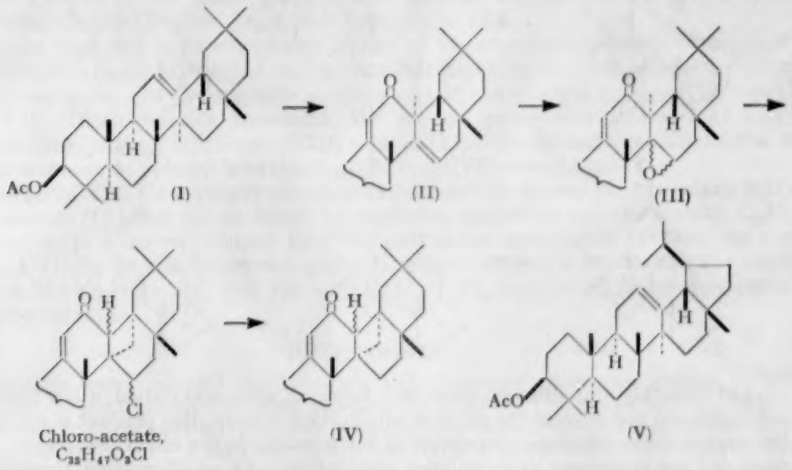
A partial synthesis of the hexacyclic triterpenoid alcohol, phyllanthol, from α-amyrin is described. The conversion of 12-oxo*iso*oursa-9(11) : 14-dien-3β-yl acetate (*iso*-α-amyradienonyl acetate) (VI) into "*iso*-α-amyradienonyl-II acetate" by means of mineral acid is shown to involve a cyclisation with the formation of a *cyclo*propane ring.

DURING a study of the complex reactions of the pentacyclic 12-oxotaraxera-9(11) : 14-dien-3β-yl acetate (II) [formerly called *iso*-β-amyradienonyl acetate or 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate], Johnston and Spring (*J.*, 1954, 1556) adduced evidence that it can be converted into hexacyclic derivatives and proposed provisional structures for these compounds. In particular, it was shown that the oxo-dienyl acetate (II) gives an oxide, $C_{32}H_{48}O_4$ (III), converted by hydrochloric acid into a chloro-acetate, $C_{32}H_{47}O_3Cl$, which on reduction yields an acetate, $C_{32}H_{48}O_3$, in which the presence of an acetate and an αβ-unsaturated ketone group and a *cyclo*alkane ring was identified. For purposes of illustration these reactions were formulated as shown.

Although α-amyrin acetate (V) (Beaton, Spring, Stevenson, and Strachan, *J.*, 1955, 2610) can be converted into 12-oxo*iso*oursa-9(11) : 14-dien-3β-yl acetate (VI) by a series of

* Part XLIV, *J.*, 1955, 3378.

reactions (Ruzicka, Rüegg, Volli, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 140) similar to those used to convert β-amyrin acetate (I) into the analogous oxo-dienyl acetate (II), a difference has been noted in the behaviour of the isomers (II) and (VI). Whereas the former is stable to prolonged treatment with hydrochloric–acetic acid mixture (Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019), 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (VI) is thereby converted into " *iso*-α-amyradienonyl-II acetate " (Ruzicka *et al.*, *loc. cit.*) which, in contrast to the parent oxo-dienyl acetate (VI), does not contain an isolated ethylene



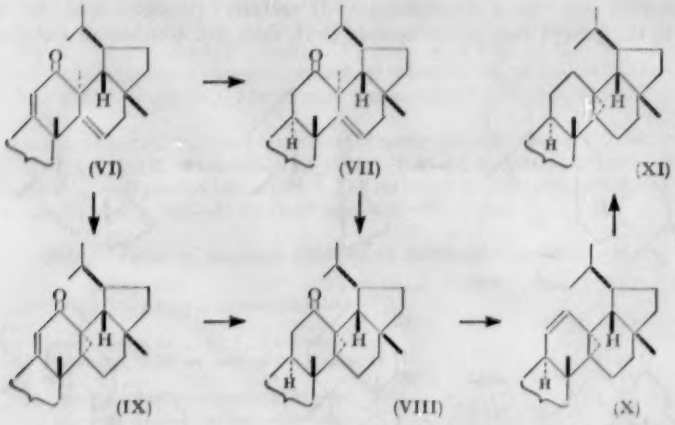
linkage. Johnston and Spring (*loc. cit.*) commented upon a resemblance between the hexacyclic acetate, $C_{32}H_{48}O_3$, derived from β-amyrin and the isomeric " *iso*-α-amyradienonyl-II acetate " and suggested that the two have analogous structures. This is equivalent to suggesting that the conversion of the acetate (VI) into " *iso*-α-amyradienonyl-II acetate " by mineral acid consists in the formation of a new *cyclo*alkane ring. This view has now been shown to be correct and, further, the precise nature of the *cyclo*alkane ring in " *iso*-α-amyradienonyl-II acetate " has been determined.

Reduction of the acetate (VI) with lithium and liquid ammonia gives 12-oxo*iso*urs-14-en-3β-ol, characterised by the preparation of its acetate (VII), which does not show the absorption spectrum of an αβ-unsaturated ketone. Its absorption in the region 2000—2200 Å and a positive reaction with tetranitromethane confirm the presence of an isolated double bond. When treated with hydrogen chloride in acetic acid, the unsaturated acetate (VII) is isomerised to 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate (VIII), the structure of which follows from the following facts. It does not give a colour with tetranitromethane in chloroform, and it does not show the ultraviolet absorption spectrum of an αβ-unsaturated ketone. Consequently its formation from (VII) consists in the formation of a new *cyclo*alkane ring. The nature of this ring was deduced from the ultraviolet absorption spectrum of (VIII) which shows a maximum at 2140 Å (ε 5500), indicating that the carbonyl group is conjugated with a *cyclo*propane ring. 12-Oxo-13 : 27-*cyclo*ursan-3β-yl acetate (VIII) was obtained also by another route. As stated above, treatment of the oxo-dienyl acetate (VI) with hydrogen chloride in acetic acid gives " *iso*-α-amyradienonyl-II acetate " which we now formulate as 12-oxo-13 : 27-*cyclo*urs-9(11)-en-3β-yl acetate (IX). Reduction of this with lithium in liquid ammonia gives, as major product, the acetate (VIII).

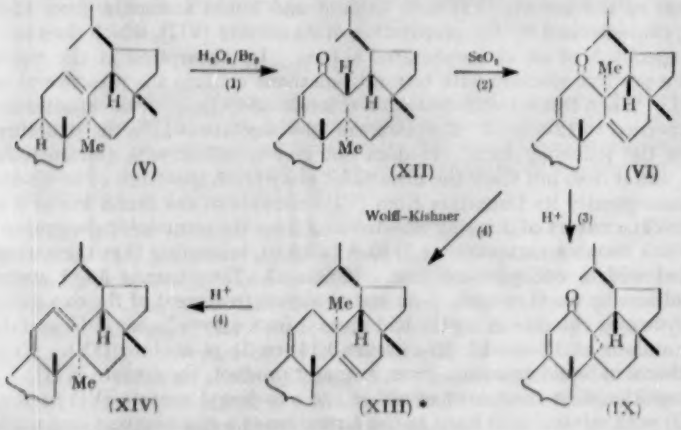
The recognition that treatment of either the oxo-dienyl acetate (VI) or the oxo-enyl acetate (VII) with mineral acid leads to the formation of a *cyclo*propane ring made possible a partial synthesis of phyllanthol, a naturally occurring triterpenoid alcohol isolated from the root bark of *Phyllanthus engleri* (Pax) by Alberman and Kipping (*J.*, 1951, 2296) and shown to be 3β-hydroxy-13 : 27-*cyclo*ursane by Barton, Page, and Warnhoff (*J.*, 1954,

2715; Barton and de Mayo, *J.*, 1953, 2178). In terms of the α-amyrin formula (V), the constitution and stereochemistry of phyllanthol are represented as in (XI).

Our first approach to a conversion of α-amyrin into phyllanthol was a modified Wolff–Kishner reduction of 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate (VIII). This reaction did



not proceed smoothly and although there was obtained, after acetylation, a low yield of a product which did not depress the m. p. of phyllanthyl acetate, this product is not homogeneous since it shows ethylenic absorption of low intensity in the ultraviolet region. The low yield did not encourage us to attempt purification. As an alternative, treatment of the acetate (VIII) with lithium aluminium hydride, followed by acetylation of the product, yielded a homogeneous acetate, $C_{32}H_{50}O_2$, which gave an orange colour with tetranitromethane and showed maximal absorption at 2250 Å (ε 4300). Because of these properties we designate this acetate 13 : 27-*cyclo*urs-11-en-3β-yl acetate (X). A related compound, 13 : 27-*cyclo*urs-11-ene-3β : 28-diol, has recently been obtained by Zürcher, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1954, **37**, 2145) by treatment of urs-12-ene-3β : 14 : 28-triol (obtained from quinovic acid) with methanesulphonyl chloride and reduction of the product



(1) Seymour, Sharples, and Spring, *J.*, 1939, 1079. (2) Ruzicka *et al.*, *loc. cit.* (3) This paper. (4) Easton and Spring, *J.*, 1955, 2120.

* It is possible that the hydrocarbon obtained by this method has the 11: 14-diene structure (Easton and Spring, *loc. cit.*).

with lithium aluminium hydride. The ultraviolet absorption spectrum of the corresponding diacetate ($\lambda_{max.}$ 2240 Å, log ε 3·64) is almost identical with that of the acetate (X).

Catalytic hydrogenation of the acetate (X) gave phyllanthyl acetate (XI), identity being confirmed by mixed m. p. and by a comparison of the infrared absorption spectra of the specimen obtained from α-amyrin and a specimen from its natural source, kindly given to us by Professor D. H. R. Barton, F.R.S. We cordially thank Dr. G. Eglinton for the infrared absorption data. This constitutes a second partial synthesis of phyllanthol from another member of the ursane group of triterpenoids, the first being a partial synthesis from quinovic acid (Zürcher, Jeger, and Ruzicka, *loc. cit.*).

In our view, the most remarkable feature of the experiments described above is the demonstration of the mobility of the carbon atom originally attached as a methyl group to $C_{(14)}$ in α-amyrin. In the requisite environment it can migrate to $C_{(13)}$ [(V) ⟶ (XII) ⟶ (VI)]. With suitable treatment, the methyl group now attached to $C_{(13)}$ will migrate back to $C_{(14)}$ [(VI) ⟶ (XIII) ⟶ (XIV)]. In different conditions the same carbon atom can be induced to bridge $C_{(13)}$ and $C_{(14)}$ [(VI) ⟶ (IX)].

The proof that "*iso*-α-amyradienonyl-II acetate" is 12-oxo-13 : 27-*cyclo*urs-9(11)-en-3β-yl acetate (IX) and the similarity between this compound and the acetate, $C_{32}H_{48}O_3$, obtained from β-amyrin suggest that the provisional formulation (IV) for the acetate $C_{32}H_{48}O_3$ (Johnston and Spring, *loc. cit.*) may require revision to 12-oxo-13 : 27-*cyclo*olean-9(11)-en-3β-yl acetate, *i.e.*, that the acetate, $C_{32}H_{48}O_3$, and its congeners may contain a *cyclo*propane ring.

Experimental

Rotations were measured in chloroform and ultraviolet absorption spectra in ethanol solutions. Grade II alumina and light petroleum (b. p. 60—80°) were used for chromatography.

12-*Oxo*-13 : 27-cyclo*urs*-9(11)-*en*-3β-*yl Acetate* (IX) ("iso-α-*Amyradienonyl*-II *Acetate*") (cf. Ruzicka, *et al.*, *loc. cit.*; Easton and Spring, *loc. cit.*).—A solution of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (3·0 g.; m. p. 221—222°, $[\alpha]_D$ +8°) in glacial acetic acid (600 c.c.) was treated with a rapid stream of dry hydrogen chloride for 40 min. and the mixture kept for 4 days and then evaporated under reduced pressure. The residue crystallised from *n*-hexane–benzene to give 12-*oxo*-13 : 27-cyclo*urs*-9(11)-*en*-3β-*yl acetate* (1·2 g.) as needles, m. p 269—270°, $[\alpha]_D$ +160°, +157° (*c*, 0·8, 1·3), $\lambda_{max.}$ 2370 Å (ε 11,000). It gives a very pale yellow colour with tetranitromethane in chloroform (Found : C, 80·2; H, 10·3. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·1%).

12-*Oxo*-13 : 27-cyclo*urs*-9(11)-*en*-3β-*ol* was obtained by hydrolysis of the acetate in the usual manner. It separates from *n*-hexane–acetone as needles, m. p. 215—216°, $[\alpha]_D$ +154°, +157° (*c*, 0·6, 1·0) (Found : C, 82·0; H, 10·6. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%). Acetylation of the alcohol in the usual way and crystallisation from *n*-hexane–benzene refurnished the acetate (IX) as needles, m. p. 268—269°, $[\alpha]_D$ +158° (*c*, 1·7).

12-*Oxo*iso*urs*-14-*en*-3β-*yl Acetate* (VII) *from* 12-*Oxo*iso*ursa*-9(11) : 14-*dien*-3β-*yl Acetate* (VI).—The acetate (VI) (8·0 g., m. p. 221—222°, $[\alpha]_D$ +7°) in dry ether (1·5 l.) was added during 7 min. with stirring to a solution obtained by adding lithium (750 mg.) to liquid ammonia (1·5 l.), and the mixture stirred for 10 min. After the addition of ammonium chloride, the product was isolated in the usual manner and refluxed for 2 hr. with 3% ethanolic potassium hydroxide. Crystallisation of the product gave 12-*oxo*iso*urs*-14-*en*-3β-*ol* (1·1 g.) as needles, m. p. 233—234°, $[\alpha]_D$ −39°, −40° (*c*, 0·8, 0·9) (Found : C, 81·3; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·7; H, 11·0%). Light absorption : ε_{3100} 2900, ε_{3150} 1600, ε_{2200} 1000. The compound gives a yellow colour with tetranitromethane. Acetylation of the alcohol gave 12-*oxo*iso*urs*-14-*en*-3β-*yl acetate* as needles (from chloroform–methanol), m. p. 227—228°, $[\alpha]_D$ −27°, −28° (*c*, 1·3, 1·1) (Found : C, 79·3; H, 10·4. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). Light absorption : ε_{3100} 2700, ε_{3150} 1300, ε_{2200} 800. The acetate gives a yellow colour with tetranitromethane.

12-*Oxo*-13 : 27-cyclo*ursan*-3β-*yl Acetate* (VIII).—(*a*) A solution of 12-oxo*iso*urs-14-en-3β-yl acetate (220 mg.) in glacial acetic acid (50 c.c.) was treated with a stream of dry hydrogen chloride for 40 min. and the mixture kept for 3 days at room temperature, then evaporated under reduced pressure. The residue crystallised from chloroform–methanol to give 12-*oxo*-13 : 27-cyclo*ursan*-3β-*yl acetate* (150 mg.) as needles, m. p. 259—261°, $[\alpha]_D$ +60° (*c*, 1·6), $\lambda_{max.}$ 2140 Å (ε 5500) (Found : C, 79·6; H, 10·7. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). This acetate does not give a colour with tetranitromethane in chloroform.

(*b*) 12-Oxo-13 : 27-*cyclo*urs-9(11)-en-3β-yl acetate (1·0 g.) in ether (150 c.c.) was added during

2 min. to a solution obtained by adding lithium (300 mg.) to liquid ammonia (200 c.c.). Stirring was continued for 3 min., and the excess of reagent decomposed by acetone. The product was isolated in the usual manner and acetylated by warm pyridine and acetic anhydride. A solution of the acetylated product in light petroleum (400 c.c.) was chromatographed on alumina (30 g.). Elution with light petroleum–benzene (9 : 1; 300 c.c.) gave fractions of m. p. 259—261° to 250—253°, which were combined (190 mg.) and recrystallised from chloroform–methanol to give an *acetate* as needles, m. p. 259—261°, $[\alpha]_D$ +47° (*c*, 1·8), ε 3100 at 2060 Å (Found: C, 76·6; 76·6, 76·6; H, 10·2, 10·1, 10·3%). The acetate gives a pale yellow colour with tetranitromethane and when it is mixed with 12-oxo-13 : 27-*cyclo*urs-9(11)-en-3β-yl acetate (m. p. 259—261°, $[\alpha]_D$ +60°) its m. p. is strongly depressed.

Continued elution of the alumina with light petroleum–benzene (9 : 1, 400 c.c.; 1 : 1, 100 c.c.) furnished fractions (284 mg.) which after crystallisation from chloroform–methanol gave 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate (155 mg.) as needles, m. p. 259—261° (no depression *), $[\alpha]_D$ +59° (*c*, 1·6), ε 4700 at 2150 Å.

The final fractions from the chromatogram were eluted with light petroleum–benzene (1 : 1, 300 c.c.) and benzene (400 c.c.). They were crystallised repeatedly from chloroform–methanol to give an *acetate* (80 mg.) as needles, m. p. 318—320°, $[\alpha]_D$ −15°, −15·5° (*c*, 1·6, 1·7), ε 4900 at 2110 Å (Found: C, 79·5; H, 10·1. $C_{32}H_{50}O_2$ requires C, 79·6; H, 10·4%). The acetate gives a faint yellow colour with tetranitromethane in chloroform.

12-*Oxo*-13 : 27-cyclo*ursan*-3β-*ol*.—A solution of 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate (100 mg.) in 3% methanolic potassium hydroxide (50 c.c.) was refluxed for 1 hr. The product, which partly separated from the hot solution, was completely precipitated by the addition of water and crystallised from chloroform–methanol to give 12-*oxo*-13 : 27-cyclo*ursan*-3β-*ol* as needles, m. p. 319—321°, $[\alpha]_D$ +51° (*c*, 0·22) (Found: C, 81·3; H, 11·25. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). Acetylation of the alcohol in the usual manner furnished 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate as needles from chloroform–methanol, m. p. and mixed m. p. 261—263°, $[\alpha]_D$ +57° (*c*, 1·0).

The relative insolubility of this alcohol was utilised to facilitate later preparations of 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate. The mixture of products obtained by reduction of 12-oxo-13 : 27-*cyclo*urs-9(11)-en-3β-yl acetate with lithium in liquid ammonia, as described above, was warmed with ether. The insoluble fraction readily gave 12-oxo-13 : 27-*cyclo*ursan-3β-ol (yield, 43%) on recrystallisation from chloroform–methanol. Acetylation of the alcohol, in the usual manner, gave 12-oxo-13 : 27-*cyclo*ursan-3β-yl acetate as needles (from chloroform–methanol), m. p. 260—261° (no depression), $[\alpha]_D$ +60° (*c*, 0·9), λ_{max} 2150 Å (ε 4700) (Found: C, 79·6; H, 10·7%).

Wolff–Kishner Reduction of 12-*Oxo*-13 : 27-cyclo*ursan*-3β-*yl Acetate* (VIII).—12-Oxo-13 : 27-*cyclo*ursan-3β-yl acetate (200 mg.) was added to a solution obtained by adding sodium (600 mg.) to freshly distilled diethylene glycol (30 c.c.), and the mixture was heated to 170—180°. Anhydrous hydrazine was distilled (in nitrogen) into the mixture until it refluxed gently at 174°. After refluxing at this temperature for 24 hr., the mixture was distilled until the temperature rose to 216°, whereafter refluxing was continued for 18 hr. Solution was not complete during the reaction. The product was isolated in the usual manner and acetylated by using pyridine and acetic anhydride. The acetylated product in light petroleum (100 c.c.) was chromatographed on alumina (7 g.). Elution with light petroleum (200 c.c.) gave a fraction (39 mg.) which was thrice crystallised from chloroform–methanol to give blades, m. p. 264—266°, $[\alpha]_D$ +36·5° (*c*, 1·2), ε_{2940} 1700. This acetate gives a pale yellow colour with tetranitromethane in chloroform, and its mixture with phyllanthyl acetate (m. p. 268—270°) had m. p. 263—268°. A mixture with (VIII) had m. p. 253—260°. In our opinion this acetate is phyllanthyl acetate contaminated with an ethylenic component. The small amount of material available did not permit its further purification. It is probable that the efficiency of the reduction is impaired by the precipitation of 12-oxo-13 : 27-*cyclo*ursan-3β-ol.

13 : 27-cyclo*Urs*-11-*en*-3β-*yl Acetate* (X) *from* 12-*Oxo*-13 : 17-cyclo*ursan*-3β-*yl Acetate* (VIII).—Lithium aluminium hydride (200 mg.) was added to a solution of the oxo-acetate (200 mg.) in dry ether (150 c.c.). After 1 hr. at room temperature, the mixture was cooled to 0° and the excess of hydride decomposed by the addition of crushed ice. The product, isolated in the usual manner, was acetylated by treatment with acetic anhydride and pyridine at room temperature for 18 hr. The acetylated product was isolated in the usual manner, and its solution in light petroleum chromatographed on alumina. Elution with light petroleum yielded a

* Here and elsewhere these words refer to a mixed m. p. with an authentic specimen.

fraction (76 mg.) which crystallised from chloroform–methanol to give 13 : 27-cyclo*urs*-11-*en*-3β-*yl acetate* (44 mg.) as plates, m. p. 224—226°, $[\alpha]_D$ +25° (*c*, 0·8), $\lambda_{max.}$ 2250 (ε 4300) (Found : C, 82·05; H, 10·8. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). It gives an orange colour with tetranitromethane.

Catalytic Hydrogenation of 13 : 27-cyclo*Urs*-11-*en*-3β-*yl Acetate* (X).—A solution of 13 : 27-*cyclo*urs-11-en-3β-yl acetate (100 mg.) in glacial acetic acid (120 c.c.) was shaken with platinum (from 100 mg. of PtO_2) and hydrogen for 2 hr. The product was isolated in the usual way and crystallised from chloroform–methanol to give phyllanthyl acetate (67 mg.) as blades, m. p. 268—272°, $[\alpha]_D$ +50°, +49° (*c*, 0·8, 1·4); this has no ultraviolet absorption and gives a pale yellow colour with tetranitromethane in chloroform. A specimen of phyllanthyl acetate, $[\alpha]_D$ +48° [from *Phyllanthus engleri* (Pax.)], separated from chloroform–methanol as blades, m. p. 268—270°; a mixture of this with the sample obtained from α-amyrin was undepressed in m. p.

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Nitramines and Nitramides. Part IX. The Acid-catalysed Decomposition of* O-*Methyl*-N-iso*propylnitramine.*

By PETER BRUCK and ALEX. H. LAMBERTON.

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The *N*- and *O*-methyl derivatives of *N-iso*propylnitramine have been adequately characterised. The decomposition of the *O*-isomer to yield nitrous oxide, together with methyl and *iso*propyl alcohol exhibits general acid-catalysis. The rate of decomposition is much greater than that of the parent *iso*propylnitramine in identical conditions, and there is no sign of any "build-up" of *iso*propylnitramine during decomposition : the process cannot, in any ordinary sense, involve hydrolysis of the *O*-alkyl compound and subsequent decomposition of the parent nitramine.

Values of $\lambda_{max.}$ and log $\varepsilon_{max.}$ in the ultraviolet spectra of some *ON*-dialkylnitramines are given in the Experimental section.

FRANCHIMONT and VAN DISSEL (*Rec. Trav. chim.*, 1894, **13**, 329) treated the potassium salt of methylnitramine with *iso*propyl iodide and obtained, by distillation at 40 mm., fractions of b. p. 60—61° and 106—108°. At that time the existence of *ON*-dialkylnitramines was unsuspected, and the lower-boiling fraction was reported as *N*-methyl-*N-iso*propyl nitramine : it still remains as such in the literature, though the boiling point recorded is anomalous. We have prepared true *N*-methyl-*N-iso*propylnitramine by methylation of the potassium salt of *iso*propylnitramine; the boiling point (108—109°/40 mm.) corresponds with their second fraction, and the constitution has been established by reduction to methyl*iso*propylamine, isolated as the toluene-*p*-sulphonamide. Franchimont and van Dissel's first fraction was presumably *N*-methyl-*O-iso*propylnitramine, which we have prepared by treatment of the silver salt of methylnitramine with *iso*propyl iodide.

Methylation of the silver salt of *iso*propylnitramine with methyl iodide yielded *O*-methyl-*N-iso*propylnitramine, together with a little (<1 part in 10) of the *N*-methyl isomeride. The use of dimethyl sulphate gave *N*- and *O*-isomers in equal proportions, and diazomethane yielded 7 parts of the *N*- to 3 parts of the *O*-compound.

Early workers (Umbgrove and Franchimont, *Rec. Trav. chim.*, 1898, **17**, 287; Backer, Ahrens Sammlung, 1912, **18**, 359) showed qualitatively that decomposition of R·N:NO·OR′ by 40% sulphuric acid yielded nitrous oxide, together with the alcohols ROH and R′OH; suitable alkyl groups in place of R, but not of R′, gave rise to olefins, and the nitrous oxide was said, on fair evidence, to be produced quantitatively. Modern work (Wright *et al.*, *Canad. J. Res.*, 1948, **26**, *B*, 130; *J. Amer. Chem. Soc.*, 1950, **72**,

* Part VIII, *J.*, 1955, 1655.

1030) has confirmed the use of sulphuric acid to distinguish *ON*- from *NN*-isomerides, but no detailed investigation of the reaction has been made.

In confirmation of the overall reaction $R{\cdot}N{:}NO{\cdot}OR' + H_2O \longrightarrow ROH + N_2O + R'OH$ we have found that the gas evolved from *O*-methyl-*N*-*iso*propylnitramine contains no elemental nitrogen; and that if the decomposition is carried out in the presence of dichromate, the oxidising agent consumed corresponds to the conversion of methyl alcohol into formic acid, and of *iso*propyl alcohol into acetone. Olefin formation (see previous paragraph) suggests that R, but not R', is liberated as an alkyl cation. We have demonstrated this by the formation, in hydrochloric acid, of RCl but not of R'Cl; requisite conditions, and results, are dealt with in the Experimental section.

The complete decomposition of *O*-methyl-*N*-*iso*propylnitramine to yield nitrous oxide has been found to be much more rapid than that of the parent *iso*propylnitramine in identical conditions, and no *iso*propylnitramine is formed during the reaction. The suggestion that the process involves hydrolysis to, and subsequent decomposition of, the *aci*-form ($Pr^i{\cdot}N{:}NO{\cdot}OH$) of the primary nitramine (Backer, *loc. cit.*) cannot be maintained, since this would imply that in the competing reactions $R{\cdot}NH{\cdot}NO_2 \rightleftharpoons R{\cdot}N{:}NO{\cdot}OH \longrightarrow R{\cdot}OH + N_2O$ the rate of decomposition must be much greater than that of equilibration, if the primary nitramine is not to accumulate in a (comparatively) stable form. But if this were so, then acidification of a salt of a primary nitramine (*e.g.*, $R{\cdot}N{:}NO{\cdot}ONa$) would yield $ROH + N_2O$, rather than $R{\cdot}NH{\cdot}NO_2$. The reaction possibly proceeds by a mechanism analogous to ester hydrolysis ($R{\cdot}N{:}NO{\cdot}OR' \xrightarrow{+H^+} R{\cdot}N{:}NO{\cdot}\overset{+}{O}HR' \longrightarrow R^+ + N_2O + R'OH$) but discussion is deferred until our measurements on a series of *ON*-dialkylnitramines have been completed.

Rates of decomposition of *O*-methyl-*N*-*iso*propylnitramine have been measured manometrically, and by observation of optical density in the ultraviolet region. In all cases the reaction was of the first order with respect to the nitramine. Table 1 shows that the methods of measurement, based respectively on the appearance of the final product (Gas) and the disappearance of the nitramine (U.V.), are in good agreement. The observed rates, in hydrochloric or sulphuric acid, are proportional to the hydrogen-ion content of the solutions, and the average catalytic constant, k_{H^+}, at 45°, is 3·6 l. mole^{-1} min.$^{-1}$. This is 2000—3000 times as large as the value of k_{H^+} for *iso*propylnitramine in aqueous sulphuric acid at the same temperature.

TABLE 1. *Decomposition of* O-*methyl*-N-iso*propylnitramine, initially* 0·05M *in aqueous acids, at* 45° ± 0·1°.

Run no.	Acid (mole l.$^{-1}$ at 20°)	$10^3[H^+]$ at 45° (calc.)	Method of measurement	First-order rate coefficient, 10^3k (min.$^{-1}$)	Catalytic constant k_{H^+} (l. mole^{-1} min.$^{-1}$)
I	0·05M-HCl	49·8	U.V.	180	3·6
II	0·025M-HCl	24·9	U.V.	87·8	3·5
III	0·01M-HCl	9·96	U.V.	35·7	3·6
IV	0·0051M-H_2SO_4	8·0	Gas	26·0	3·3
V	0·0033M-H_2SO_4	5·4	Gas	17·5	3·2
VI	0·005M-HCl	4·98	U.V.	16·5	3·3
VII	0·002M-H_2SO_4	3·5	Gas	12·0	3·4
VIII	0·002M-HCl	1·99	Gas	8·0	4·0
IX	0·001M-H_2SO_4	1·86	Gas	7·1	3·8
X	0·001M-HCl	0·996	Gas	4·0	4·0
XI	0·001M-HCl	0·996	U.V.	3·5	3·5
XII	0·0005M-H_2SO_4	0·97	Gas	4·0	4·1

Runs XIII *and* XIV.—A solution (0·05M) of *O*-methyl-*N*-*iso*propylnitramine in distilled water gave no measurable gas evolution during 4 days at 45°: catalysis by water cannot, therefore, be recognised at this temperature. A solution (0·05M) of *iso*propylnitramine in 0·5M-H_2SO_4 ($10^3[H^+]$ = 501 at 45°) gave, by gas evolution at 45°, a first-order coefficient of $0·7 \times 10^{-3}$ min.$^{-1}$, indicating a k_{H^+} value of about 0·0014 l. mole^{-1} min.$^{-1}$.

Table 2 extends, for hydrochloric acid, the field of measurement covered by Table 1. Runs XIX—XXII are not fully in accordance with expectation: they show a slight (5%) "drift" and, since a spontaneous (water-catalysed) reaction is observable at 85°, a drift of about the same extent, but in the opposite sense, might be expected. The results,

however, show that, at suitable temperatures, the rate of decomposition is proportional to $[H^+][Pr^i{\cdot}N{:}NO{\cdot}OMe]$ to within 10% over a 2000-fold range of concentration of hydrochloric acid. The average values of k_{H^+} (after allowance, at 85°, for water catalysis) are 0·39 and 89 l. mole^{-1} min.$^{-1}$ at 25° and 85° respectively. A plot of log k_{H^+} against 1/Temp. (°K) gives points which are not precisely linear; the observed rate coefficients at 25°, 45°, and 85° are respectively 8% less, 8% more, and 16% less than those values which would give points on what we consider to be the best line. In view of the different methods of measurement, and the wide range of solvent concentration and temperature, these divergences are perhaps to be expected; and the only valid conclusion at present is that the activation energy, E, is about 20,000 cal.

Catalysis by acetic acid (and therefore, probably, by acids in general) has been demonstrated by the manometric measurements at 85° which are given in Table 3. The values of the first-order rate coefficient are linear with respect to [AcOH] and show an intercept of $3{\cdot}7 \pm 0{\cdot}2 \times 10^{-3}$ min.$^{-1}$ at [AcOH] = 0. The intercept is greater than might be attributed solely to k_{H^+} in these solutions, and the remainder of the rate is presumably due to catalysis by water molecules. We tried to verify this by direct observation: the results, though of the right order (runs nos. XXVII—XXIX, $k = 2{\cdot}3$, 1·1, and $1{\cdot}6 \times 10^{-3}$ min.$^{-1}$), were not consistent enough for quantitative use. An experiment with 0·01M-sodium hydroxide (Table 3, run XXX) showed that there was no pronounced basic catalysis, and we assumed that, if the hydroxyl ion was ineffective, variations in the

TABLE 2. *Decomposition of* O-*methyl*-N-iso*propylnitramine, initially* 0·05M *in hydrochloric acid, at various temperatures.*

Run No.	Temp. (±0·1°)	Acid (mole l.$^{-1}$ at 20°)	$10^3[H^+]$ (calc.)	Method of measurement	First-order rate coefficient, 10^3k (min.$^{-1}$)	Catalytic constant, k_{H^+} (l. mole^{-1} min.$^{-1}$)
XV	25°	0·54	540	U.V.	223	0·41
XVI	25	0·108	108	U.V.	40·4	0·37
XVII & XVIII	25	0·05	50	U.V.	19·1	0·38
See Table 1	45	0·05—0·001	—	Gas & U.V.	—	3·6
XIX	85	0·001	0·969	Gas	91·6	95 *
XX & XXI	85	0·0005	0·485	Gas	45·0	93 *
XXII	85	0·00025	0·242	Gas	21·6	89 *

* Without allowance for catalysis by water.

TABLE 3. *Decomposition of* O-*methyl*-N-iso*propylnitramine, initially* 0·05M, *at* 85° ± 0·1°.

Run no.	Composition of solvent, at 20°	First-order rate coefficient, 10^3k (min.$^{-1}$) *
XXIII	0·1M-AcOH and AcONa	7·6
XXIV	0·075M-AcOH and AcONa + 0·025M-NaCl	6·4
XXV	0·05M-AcOH and AcONa + 0·05M-NaCl	5·7
XXVI	0·025M-AcOH and AcONa + 0·075M-NaCl	4·7
XXX	0·01M-NaOH	1·1
XXXV	0·1M-AcONa	1·5
XXVI	0·025M-AcONa	1·4
XXXVII	0·025M-AcONa + 0·075M-NaCl	1·4

* In all cases by manometric measurements.

concentration of acetate ions would have no significant influence on the rate. Our referees, however, were of the opinion that this assumption should be experimentally investigated, and we have therefore (subsequently) carried out the runs (XXXV—XXXVII) tabulated in Table 3. These (in which hydrolysis does not produce a significant quantity of acetic acid) show that variations in the concentration of acetate ions, or of sodium chloride, do not produce changes outside the probable experimental error; that the spontaneous (water-catalysed) rate is $1{\cdot}4 \pm 0{\cdot}2 \times 10^{-3}$ min.$^{-1}$ at 85°; and that the variations in runs XXIII—XXVI may be attributed with confidence to catalysis by acetic acid. For comparison with the k_{H^+} value of 89, k_{AcOH} is $4{\cdot}0 \times 10^{-2}$ and k_{H_2O} $2{\cdot}6 \times 10^{-5}$, all at 85° and in units of l. mole^{-1} min.$^{-1}$. These figures are in agreement with the Brønsted relation between

catalytic coefficient and dissociation constant : probable values being used for the dissociation constants at 85°, the agreement is as good as, if not better than, that found (Brønsted and Guggenheim, *J. Amer. Chem. Soc.*, 1927, **49**, 2582) for the acid-catalysed mutarotation of glucose.

The difference ($2{\cdot}3 \pm 0{\cdot}4 \times 10^{-3}$ min.$^{-1}$) between the intercept for [AcOH] = 0 and the spontaneous rate seems not improbable for the catalytic influence of [H^+] in the buffer solutions used. No precise figures relevant to 85° were found, but the following approximation is of interest. From MacInnes's figures (" The Principles of Electrochemistry," Reinhold, New York, 1939, pp. 205, 278) the hydrogen-ion content of an acetic acid buffer (AcOH and AcONa, both 0·1N) exceeds the numerical value of the dissociation constant of acetic acid by 0·5, 0·55, and $0{\cdot}6 \times 10^{-5}$, at, respectively, 12°, 25°, and 38°. If this difference is at least maintained, then, from an extrapolated value of $1{\cdot}3 \times 10^{-5}$ for the dissociation constant of acetic acid at 85°, [H^+] in the buffer of run no. XXIII would be $1{\cdot}9 \times 10^{-5}$; k_{H^+} being taken as 89, the resultant first-order rate would be $1{\cdot}7 \times 10^{-3}$ min.$^{-1}$. This approximation makes some attempt to allow for secondary salt effects : the residual difference of $0{\cdot}6 \times 10^{-3}$ min.$^{-1}$ is scarcely beyond the sum of possible experimental errors, and might well be reduced if primary salt effects were taken into consideration. It may be added that the precise extent of hydrogen-ion catalysis is irrelevant to arguments based on such (run nos. XXIII—XXVI) " isohydric " salt solutions. All that is necessary is to show—as we believe we have done—that any unexplained effect is relatively small.

Experimental

Reaction rates were evaluated on the basis of natural logarithms. In calculating hydrogen-ion concentrations in sulphuric acid use was made of Hamer's work (*J. Amer. Chem. Soc.*, 1934, **56**, 860). For other solvents corrections have been made on the assumption that these dilute solutions showed the same expansion as water over the range 20—85°.

All compounds reported as *ON*-dialkylnitramines gave an immediate evolution of gas on treatment with 40% sulphuric acid at room temperature. It appears (p. 4002) that they can also be distinguished spectroscopically from their *NN*-isomerides. The silver salts employed in alkylation were precipitated from water by the action of a slight excess of silver nitrate on the ammonium or *iso*propylammonium salts of the nitramines : they were collected, washed successively with water, acetone, and ether, and " dried " *in vacuo*. Refractive indices were measured with an Abbé refractometer at room temperature (18—21°).

N-*Methyl*-N-*isopropylnitramine*.—*iso*Propylnitramine (5 g.), potassium hydroxide (2·8 g.), methyl iodide (10 g.), and dry ethanol (75 ml.) were shaken, at room temperature, for two days. The resultant potassium iodide was collected, and the filtrate concentrated by distillation of ethanol at 60°/300 mm. A further small precipitate of potassium iodide was removed, and the residual oil distilled to yield fractions of b. p. 59—60°/40 mm. (0·5 g.) and 107°/40 mm. (3·4 g.). The lower-boiling fraction (*O*-methyl isomer) is obtained in better yield from the silver salt of *iso*propylnitramine. The higher-boiling fraction was washed in ethereal solution with aqueous sodium hydrogen carbonate and distilled, after removal of ether, to yield N-*methyl*-N-*isopropylnitramine*, b. p. 85—86°/10 mm., n_D 1·456 (Found : C, 40·4; H, 8·7; N, 23·6. $C_4H_{10}O_2N_2$ requires C, 40·7; H, 8·5; N, 23·7%).

Characterisation of N-*Methyl*-N-*isopropylnitramine*.—The nitramine (1 g.) was heated under reflux for 5 hr. with granulated tin (6 g.) and hydrochloric acid (15 ml. of conc.). Excess of tin was collected, and the filtrate concentrated to 5 ml. The amine was liberated by treatment with sodium hydroxide (20 ml. of 40%) in a semimicro-Kjeldahl apparatus, and was steam distilled into hydrochloric acid. Evaporation yielded crops of the hydrochloride of methyl-*iso*propylamine (0·8 g. of hygroscopic material). The hydrochloride (0·3 g.), dissolved in sodium hydroxide (1 ml. of 20%), was treated with toluene-*p*-sulphonyl chloride (1 g.) in acetone. The resultant precipitate was collected, washed with dilute aqueous sodium hydroxide and with water, dried, and crystallised from acetone to yield stout prisms of *N*-methyl-*N*-*iso*propyltoluene-*p*-sulphonamide, identified by m. p. (78—79° ; Boon, *J.*, 1947, 311, gave 78°) and mixed m. p. with authentic material (Found : S, 13·7. Calc. for $C_{11}H_{17}O_2NS$: S, 14·1%), prepared from *iso*propylamine by von Braun's method (*Ber.*, 1928, **61**, 1428). The intermediate N-*isopropyltoluene*-p-*sulphonamide* has been mentioned by Boon (*loc. cit.*) and others, but has not been formally described: it crystallised in stout prisms, m. p. 48—49°, from acetone (Found : C,

56·2; H, 7·1; S, 14·7. $C_{10}H_{15}O_2NS$ requires C, 56·3; H, 7·0; S, 15·0%). The dialkylsulphonamide, m. p. 78°, was also obtained by direct sulphonylation of methyl*iso*propylamine.

O-*Methyl*-N-iso*propylnitramine*.—The silver salt of *iso*propylnitramine (20 g.) was refluxed for 1½ hr. with methyl iodide (20 g.) in ether (100 ml.), and the mixture then shaken, at room temperature, for 24 hr. Silver iodide (18 g.) was collected, and the filtrate, after removal of ether through a fractionating column, was distilled to yield fractions of b. p. 59—61°/40 mm. (5 g.) and 106—108°/40 mm. (0·4 g.). The higher-boiling fraction was the *N*-methyl isomer (see p. 4000). The lower-boiling fraction was redistilled to yield O-*methyl*-N-iso*propylnitramine*, b. p. 59°/40 mm., n_D 1·428 (Found: C, 41·2; H, 8·3. $C_4H_{10}O_2N_2$ requires C, 40·7; H, 8·5%).

Methylation of iso*Propylnitramine by Dimethyl Sulphate and by Diazomethane*.—(*a*) *iso*Propylnitramine (2·5 g.) was dissolved in aqueous potassium hydroxide (1·4 g. in 20 ml. of water), and dimethyl sulphate (3·8 g.) added dropwise with constant shaking. Extraction with ether and subsequent distillation yielded fractions of b. p. 60—61° (0·6 g.) and 108—109° (0·5 g.) at 40 mm., showing a ratio of 6 : 5 for *O*- to *N*-methylation. (*b*) An ethereal solution of diazomethane (from 20 g. of *N*-methyl-*N*-nitroso-*N'*-nitroguanidine; McKay, *J. Amer. Chem. Soc.*, 1947, **69**, 3028) was added portionwise to *iso*propylnitramine (10 g. in 50 ml. of ether) until no further discharge of colour took place. The solution was distilled to remove ether and yield fractions of b. p. 58—65° (2·3 g.) and 108—110° (6·1 g.) at 40 mm., showing a ratio of 23 : 61 for *O*- to *N*-methylation.

N-*Methyl*-O-iso*propylnitramine*.—The silver salt of methylnitramine (10 g.) was refluxed for 6 hr. with *iso*propyl iodide (10 g.) in ether (200 ml.). Silver iodide (12·4 g.) was collected, and the filtrate, after removal of ether and excess of *iso*propyl iodide through a fractionating column, was distilled (2·5 g. at 57—61°/40 mm.: cf. Franchimont and van Dissel, *loc. cit.*) and redistilled to yield N-*methyl*-O-iso*propylnitramine*, b. p. 39—40°/20 mm. (Found: C, 40·2; H, 8·4. $C_4H_{10}O_2N_2$ requires C, 40·7; H, 8·5%).

O-*Methyl- and* N-*Methyl*-N-neo*pentylnitramines*.—The silver salt of *neo*pentylnitramine (8 g.) was refluxed for 4 hr. with methyl iodide (22 g.) in ether (150 ml.). After removal of silver iodide, methyl iodide, and ether, distillation yielded a liquid (2·5 g. of b. p. 69—73°/17 mm.) and a solid residue (b. p. >100°/17 mm.). Redistillation of the liquid yielded O-*methyl*-N-neo*pentylnitramine*, b. p. 63—65°/15 mm. (Found: C, 49·8; H, 9·7. $C_6H_{14}O_2N_2$ requires C, 49·3; H, 9·6%). The residue of the initial distillation was warmed with 40% sulphuric acid to destroy any remaining *O*-alkyl compound, and extracted with ether. Evaporation and crystallisation from aqueous ethanol yielded the isomeric N-*methyl*-N-neo*pentylnitramine* (0·2 g.) as lustrous needle-like plates, m. p. 65—66° (Found: C, 49·6; H, 9·6%).

ON-*Dimethyl- and* ON-*Diiso*propyl-*nitramine*.—These were prepared by methods generally similar to that used for *N*-methyl-*O-iso*propylnitramine. The dimethyl compound (Found: C, 27·0; H, 6·6. Calc. for $C_2H_6O_2N_2$: C, 26·7; H, 6·7%) had b. p. 113—115° (Franchimont and Umbgrove, *Rec. Trav. chim.*, 1896, **15**, 218, gave b. p. 112°). The di*iso*propyl compound (Found: C, 49·6; H, 9·6. Calc. for $C_6H_{14}O_2N_2$: C, 49·3; H, 9·6%) had b. p. 58—61°/18 mm. (Thomas, *ibid.*, 1890, **9**, 82, gave b. p. 55—57°/10 mm.; for identification as the *ON*-compound see Wright, *Canad. J. Res.*, 1948, **26**, *B*, 292, who gave b. p. 52—53°/10 mm.).

Gas Evolution from O-*Methyl*-N-iso*propylnitramine: Absence of Elemental Nitrogen*.—A sample of the nitramine was decomposed by means of 0·5M-sulphuric acid. The evolved gas was swept out by a stream of carbon dioxide, and collected over a concentrated solution of potassium hydroxide. Of 0·87 molecular proportion collected, less than 2% was insoluble in ethanol. Details of the method have been given by Barrott, Denton, and Lamberton (*J.*, 1953, 1998).

Decomposition of O-*Methyl*-N-iso*propylnitramine in Presence of Potassium Dichromate*.—Aqueous potassium dichromate (25 ml. of 0·5N) and sulphuric acid (25 ml. of 40%) were added to a weighed sample (*ca.* 2 mmole) of the nitramine. Samples (5 ml.) were withdrawn at intervals and run into potassium iodide solution. Similar experiments were carried out with *iso*propylnitramine, and with purified methyl and *iso*propyl alcohols. Titration of the liberated iodine with thiosulphate showed final values, in terms of equivalents of oxygen per molecule, of 8·05 for $Pr^i{\cdot}N(NO){\cdot}OMe$, 2·05 for $Pr^i{\cdot}NH{\cdot}NO_2$, 2·00 for Pr^iOH, and 6·05 for MeOH; but no useful conclusions could be drawn from the rate of oxidation.

Formation of Alkyl Chlorides during Decomposition.—A weighed sample of the nitramine (*ca.* 1 mmole) was heated under reflux on a steam-bath with a weighed quantity (*ca.* 1 g.) of 1·0M-hydrochloric acid. To ensure complete decomposition, *ON*-dialkylnitramines were heated for 2 hr., primary nitramines for 4—6 hr. The resultant solution was diluted, and the condenser washed down, with distilled water; residual acidity was determined by means of standard

potassium hydroxide, and ionisable chlorine by subsequent titration with mercuric nitrate, sodium nitroprusside being used as indicator. Results (Table 4) have been calculated on the basis of the overall equation $R{\cdot}N{:}NO{\cdot}OR' + HCl \longrightarrow RCl + N_2O + R'OH$ (R = alkyl, R' = alkyl or H). Control experiments with alcohols, and the lack of any halide formation from *O*-alkyl groups, showed that the reaction cannot proceed by formation of alcohol and subsequent esterification. Positive results suggest the formation of alkyl cations, but nil values do not disprove this, except when the same alkyl group produces alkyl chloride from an *N*-, but not from an *O*-linkage. Two factors are involved in the production of RCl: the formation of R^+, and its behaviour in its natal environment.

Evidence Against the Formation of iso*Propylnitramine during the Decomposition of* O*-Methyl-*N*-iso*propylnitramine.*—A solution of *O*-methyl-*N*-*iso*propylnitramine (initially 0·038M in 0·005M-hydrochloric acid, at 20°) was kept at 45°, and samples (5 ml.) withdrawn at once, and after time intervals known to correspond to 10, 20, 30, 40, 50, 60, 75, and 100% decomposition. These were titrated with standard (*ca.* 0·01M) sodium hydroxide. In all cases the titre was 2·65 ± 0·05 ml. No decomposition of *iso*propylnitramine can be detected in similar conditions of time, temperature, and acidity; any *iso*propylnitramine formed should therefore remain

TABLE 4. *Formation of alkyl chlorides (conditions given in the relevant experimental section).*

Compound	Yield (%) by determn. of: H^+	Yield (%) by determn. of: Cl^-	Compound *	Yield (%) by determn. of: H^+	Yield (%) by determn. of: Cl^-
MeN:NO·OMe	45·6, 47·5	45·0, 47·0	$C_5H_{11}{\cdot}N{:}NO{\cdot}OMe$	Nil	Nil
MeN:NO·OPr^i	47·2, 45·4	47·9, 44·7	$MeNH{\cdot}NO_3$ †	51	50
Pr^{i}N:NO·OMe	3·7	4·3	$Pr^iNH{\cdot}NO_3$ †	3·3	3·7
Pr^{i}N:NO·OPr^i	3·0	4·0	$C_5H_{11}{\cdot}NH{\cdot}NO_3$	Nil	Nil

* C_5H_{11} = *neo*Pentyl.
† In good agreement with earlier work (Barrott, Denton, and Lamberton, *loc. cit.*).

undecomposed, and augment the sodium hydroxide titre. A yield of 1% of *iso*propylnitramine would have raised the titre by 0·19 ml.

Measurement of Reaction Rates.—The manometric technique has been described by Barrott, Denton, and Lamberton (*loc. cit.*). In the optical technique 5 ml. of pre-warmed acid were added to a pre-warmed solution of the nitramine in water to give, on admixture, solutions of the concentrations reported. Samples (0·5 ml.) were withdrawn, run into cold 0·05M-sodium acetate (20 ml.), and then made up to 25 ml. This effectively stops the decomposition, since the optical density was found to remain constant for periods of up to 24 hr. at room temperature. The solutions were examined in a Beckman quartz spectrophotometer. The rates reported are the mean of those derived from separate logarithmic plots of optical density at 230 and 235 mμ. The opacity of sodium acetate prevented readings at the head (213—215 mμ) of the absorption band.

Measurements of Reaction Rates in Bisulphate and Chloroacetate Buffers.—In preliminary work some measurements were made by the manometric technique at 45°. The large difference between runs XXXI and XXXII is probably due mainly to catalysis by HSO_4^-; the difference between runs XXXIII and XXXIV may be due to catalysis, or may be simply a salt effect. Observed first-order rate coefficients are given in units of 10^3k(min.$^{-1}$): run XXXI in 0·1M-$NaHSO_4$ and -Na_2SO_4, 42·8; run XXXII in 0·01M-$NaHSO_4$ and -Na_2SO_4, 11·2; run XXXIII in 1·0M-$CH_2Cl{\cdot}CO_2H$ and -$CH_2Cl{\cdot}CO_2Na$, 14·7; run XXXIV in 0·1M-$CH_2Cl{\cdot}CO_2H$ and -$CH_2Cl{\cdot}CO_2Na$, 8·3.

Ultraviolet Spectra of ON- *and* NN-*Dialkylnitramines.*—The spectra of the *ON*-compounds showed (in water) maximum absorption at shorter wavelengths (213—215 mμ) than those reported (230—250 mμ; in organic solvents) for *NN*-dialkylnitramines in general (Jones and Thorn, *Canad. J. Res.*, **1949**, **27**, *B*, 828): MeN:NO·OPr^i, $\lambda_{max.}$ (in H_2O) 213 mμ (log ε 3·81); Pr^{i}N:NO·OMe, $\lambda_{max.}$ (in H_2O) 213 mμ (log ε 3·70); Pr^{i}N:NO·OPr^i, $\lambda_{max.}$ (in H_2O) 215 mμ (log ε 3·81); *neo*-$C_5H_{11}{\cdot}N{:}NO{\cdot}OMe$, $\lambda_{max.}$ (in H_2O) 213 mμ (log ε 3·83); $MePr^iN{\cdot}NO_2$, $\lambda_{max.}$ (in 16% EtOH) 238 mμ (log ε 3·81).

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The Site of the Hydroxyl Groups in Lycorine.

By S. Takagi, W. I. Taylor, S. Uyeo, and H. Yajima.

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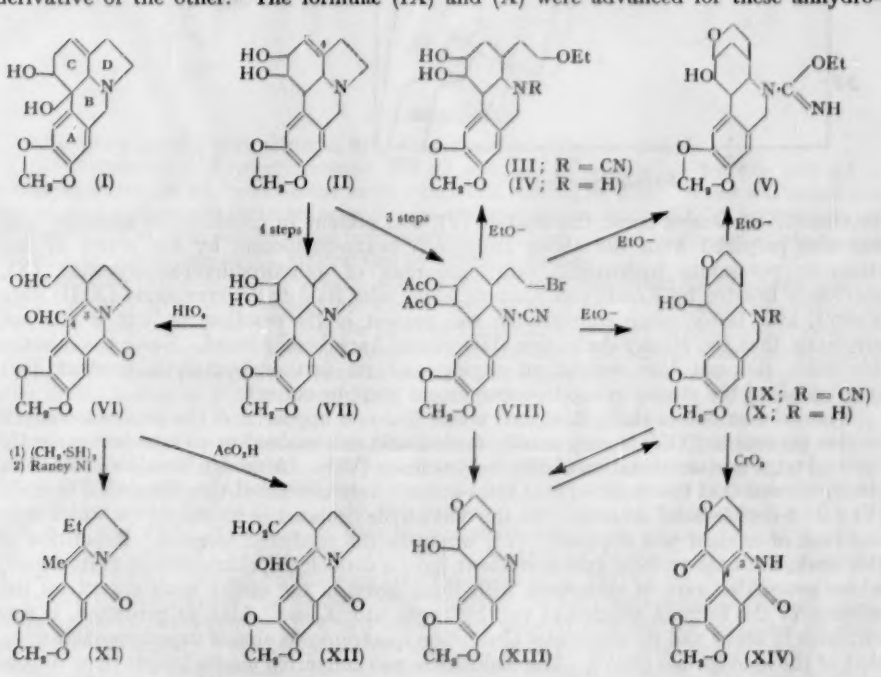
The glycol cleavage product of dihydrolycorinone is now shown to be a 4-acyl*iso*carbostyril derivative, as is also one of the degradation products of diacetyl-ω-bromo-*N*-cyanodihydro*seco*lycorine. These results receive a satisfactory interpretation on the basis of formula (II) for lycorine, which has a disecondary glycol grouping.

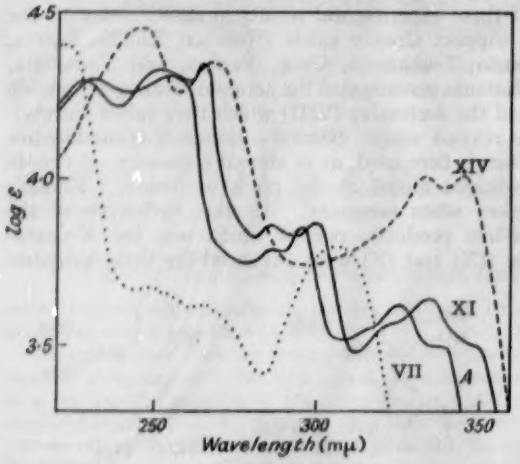
Wenkert (*Chem. and Ind.*, 1954, 1175), in the light of his reinterpretation of some of Kondo's work (Kondo and Katsura, *Ber.*, 1939, **72**, 2083; 1940, **73**, 112), suggested that lycorine must contain the secondary-tertiary glycol grouping shown in (I). There is however an alternative explanation of these experimental results in agreement with the structure (II) for which considerable support already exists (Humber, Kondo, Kotera, Takagi, Takeda, Taylor, Thomas, Tsuda, Tsukamoto, Uyeo, Yajima, and Yanaihara, *J.*, 1954, 4622). In 1939, Kondo and Katsura investigated the action of cyanogen bromide on diacetyldihydrolycorine and obtained the derivative (VIII) which they called diacetyldihydrolycorinebromocyanide but the revised name, diacetyl-ω-bromo-*N*-cyanodihydro-*seco*lycorine seems more appropriate (*seco* is here used, as in steroid chemistry, to denote ring fission with addition of two hydrogen atoms at the point of fission); Kondo's terminology has been rationalised below when necessary. Alkaline hydrolysis of the *seco*-compound afforded two bromine-free products, one of which was the *N*-cyano-derivative of the other. The formulæ (IX) and (X) were advanced for these anhydro-



products based on ultimate analyses, formation of a monoacetate, and the fact that the keto-lactam obtained on oxidation was shown not to have a methylene group adjacent to the carbonyl moiety. The keto-lactam was soluble in alkali and reprecipitated unaltered

after acidification and could be *N*-methylated by base and methyl sulphate, then becoming insoluble in alkali. This behaviour was clearly that of an *iso*carbostyril, as was partially recognised by these authors (Kondo and Katsura, *Ber.*, 1939, **72**, 2084, footnote 7), but they put forward the unacceptable structure (XIV; 3 : 4-double bond saturated) for the keto-lactam. Their analytical results as well as ours were in agreement with the *iso*carbostyril formulation (XIV) with which the infrared absorption was consistent, *i.e.*, absence of isolated carbonyl or hydroxyl bands, and presence of a broad band at 1660 cm.$^{-1}$ (overlapping conjugated keto- and lactam groupings). The ultraviolet absorption spectrum (curve XIV) was similar to that of 5 : 6-methylenedioxy*iso*carbostyril (curve *A*) in the long wavelength region, as expected, but quite different from that of corresponding dihydro*iso*-carbostyril, dihydrolycorinone (curve VII).

By treating the *seco*-compound (VIII) with potassium hydroxide in dry ethanol, we have isolated four other compounds besides the expected anhydro-*N*-cyanodihydro*seco*-



(*A*) 6 : 7-*Methylenedioxyisocarbostyril.*
(VII) *Dihydrolycorinone.*
(XI) *Ethyl compound from the dialdehyde.*
(XIV) *Keto-lactam.*

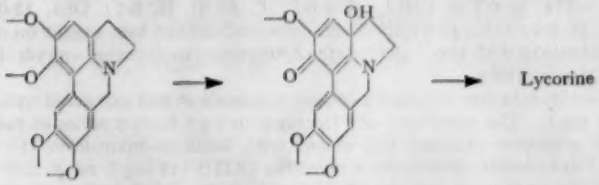
lycorine (IX). One of these, the imidate (V), was present in considerable quantity and was also prepared from the above anhydro-*N*-cyano-compound by the action of hot ethanolic potassium hydroxide. Small amounts of anhydrodihydro*seco*lycorine (X), previously isolated by Kondo and Katsura, along with its dehydro-compound (XIII) were present, and, lastly, since ethoxide ion was present in the reaction medium it was not surprising that the ethoxy-derivative (III) should have been formed. Since the ethoxy-derivative did not lose weight on drying and its further hydrolysis product (IV) still contained the ethoxy-group this assignment must be correct.

From the oxidative study described above it would appear that the oxo*iso*carbostyril residue present in (XIV) is very readily formed and this enabled us to interpret correctly the lead tetra-acetate oxidation of dihydrolycorinone (VII). Although Kondo and Katsura (1940) showed that two mols. of lead tetra-acetate were consumed they suggested formula (VI; 3 : 4-double bond saturated) for the dialdehyde (isolated as its oxime) for which only one mol. of oxidant was required; (VI) would be the predicted formula. Repetition of this work, but with periodic acid as oxidant, gave a dialdehyde, characterised as its oxime, whose properties were in agreement with those given in the earlier work except for the revision of the formula which had two hydrogen atoms less. Also, as predicted, it was insoluble in alkali and its ultraviolet absorption spectrum was almost superimposable upon that of the keto-lactam (XIV). The dialdehyde was converted *via* its bis(ethylene dithio-ketal), followed by desulphurisation with Raney nickel, into the ethyl derivative (XI) whose ultraviolet absorption spectrum (curve XI) exhibited the expected bathochromic shift in the 350-mμ region relative to that of 6 : 7-methylenedioxy*iso*carbostyril (curve *A*). Owing to the paucity of material we were unable to reinvestigate the oxidation of the dialdehyde

(VI) with peracetic acid but the recorded analytical data are in agreement with those for the aldehydo-acid (XII). No skeletal changes have occurred in the formation of dihydrolycorinone since lithium aluminium hydride reduction gave back the starting material, dihydrolycorine.

It should be noted that for ether formation in (IX) and (X) the hydroxyl group and the ethylene residue in (VIII) must lie on the same side of ring C, and if the B/C ring junction is *trans* and the hydroxyl group equatorial (Humber *et al.*, *loc. cit.*) this would mean that in dihydrolycorine ring D is *trans* fused to ring C, which would be unusual for an octahydroindole. For this reason lycorine is now regarded as having a *cis*-fused B/C ring junction, but the unequivocal solution of this stereochemical problem must await further work.

The structure of lycorine as well as that of lycorenine (Kitagawa, Taylor, Uyeo, and Yajima, *J.*, 1955, 1066) fit well into Wenkert's scheme for the biogenesis of the pyrrocoline alkaloids (*Chem. and Ind.*, 1953, 1088) but not with his revision (Wenkert and Hansen, *ibid.*, 1954, 1262). The latter scheme was put forward to conform with his ideas as to the structures of these alkaloids and to accommodate Robinson's objection (*ibid.*, 1953, 1317) in the former to the final step, reduction of the aromatic nucleus. However the formation of ring C in lycorine from an aromatic ring may simply be that as a consequence of further oxidation the ring becomes readily reducible, as in the example shown below.



Experimental

Absorption spectra were taken in 95% ethanol unless otherwise stated.

Dihydrolycorine.—Dihydrolycorinone (0·1 g.) and lithium aluminium hydride (0·2 g.) in tetrahydrofuran (30 ml.) were heated under reflux with stirring for 5 hr. Water was added and the reaction mixture was extracted several times with chloroform, dried (K_2CO_3), and evaporated to dryness. The basic portion of the residue crystallised from ethanol to give colourless needles (25 mg.), m. p. 248° (decomp.), undepressed by dihydrolycorine.

Dialdehyde (VI).—Aqueous periodic acid (0·1M; 60 ml.) was added to dihydrolycorinone (0·3 g.) in 20% acetic acid (60 ml.) and kept at 40—50° for 5 hr. The mixture was extracted with ethyl acetate (5 × 60 ml.), and the combined extracts were dried (K_2CO_3) and evaporated to dryness in an atmosphere of carbon dioxide. Trituration of the residue with methanol gave crystals which were recrystallised from the same solvent, affording the *dialdehyde* (32 mg.) which after drying had m. p. 212° (decomp.), $[\alpha]_D$ +101° (*c* 0·4 in EtOH) (Found, on a sample dried *in vacuo* over P_2O_5 at 110° for 8 hr.: C, 64·5; H, 4·6. $C_{16}H_{19}O_5N$ requires C, 64·2; H, 4·4%). The infrared absorption spectrum showed bands in the carbonyl region at 1730, 1661 (shoulder), 1639, and 1613 cm.$^{-1}$ (shoulder), and the ultraviolet absorption spectrum had $\lambda_{max.}$ in 95% EtOH 249, 266, 309, 332, and 346 mμ (log ε 4·40, 4·36, 3·86, 3·96, and 3·97), and in 0·001N-ethanolic potassium hydroxide $\lambda_{max.}$ 250, 264 (inflexion), 300, 330, and 344 mμ (log ε 4·32, 4·21, 3·79, 3·72, and 3·67). The dioxime after four crystallisations from ethanol had m. p. 252—253° (decomp.) (Found: C, 58·1, 57·6; H, 4·8, 4·7; N, 12·5. Calc. for $C_{16}H_{15}O_5N_3$: C, 58·4; H, 4·6; N, 12·8%). Kondo and Katsura (1940) recorded m. p. 233° for the dioxime.

Dialdehyde Bis(ethylene Dithioketal).—The aldehyde (32 mg.), ethanedithiol (0·3 ml.), and boron trifluoride–ether complex (0·2 ml.) were gently warmed with stirring and after 10 min. methanol was added. The precipitate (35 mg.), m. p. 247—249° after crystallisation from ethanol, gave the pure *derivative*, m. p. 255° (Found: C, 53·4, 53·1; H, 4·6, 4·6; S, 28·1. $C_{20}H_{31}O_3NS_4$ requires C, 53·2; H, 4·7; S, 28·4%).

Desulphurisation. The bisdithioketal (50 mg.), Raney nickel (7 g.), and dry methanol (100 ml.) were refluxed for 8 hr. After filtration from the catalyst and evaporation under reduced pressure the resulting oil was chromatographed over activated alumina in benzene.

After initial elution of a small amount of oil the pure *compound* (XI) was obtained from the succeeding fractions which on crystallisation from acetone gave colourless needles (29 mg.), m. p. 153—154°, $[\alpha]_D$ +11·1° (*c*, 2·0 in EtOH) (Found: C, 70·9; H, 6·2; N, 5·1; *C*-Me, 10·4, 7·8. $C_{16}H_{17}O_3N$ requires C, 70·8; H, 6·3; N, 5·2; 2*C*-Me, 11·1%). The ultraviolet absorption spectrum had $\lambda_{max.}$ 229, 250, 265, 286, 300, 322 (inflexion), 335, and 350 mμ (inflexion) (log ε 4·30, 4·34, 4·35, 3·86, 3·87, 3·56, 3·64, and 3·51).

*Diacetyl-ω-bromo-*N*-cyanodihydrosecolycorine* (VIII).—Equal quantities of diacetyl-lycorine and cyanogen bromide were heated under reflux in dry benzene to yield the *seco*-compound, m. p. 177—178°, $[\alpha]_D$ −71·6° (*c* 0·6 in $CHCl_3$) (Found: C, 52·7; H, 4·9. Calc. for $C_{21}H_{23}O_6N_2Br$: C, 56·2; H, 4·8%). It reacted only slowly with silver nitrate solution.

Action of Base on the seco*-Compound* (VIII).—A solution of the *seco*-compound (0·5 g.) and potassium hydroxide (1·3 g.) in dry ethanol (25 ml.) was kept at room temperature for 4 hr. after which carbon dioxide was introduced, the precipitated potassium carbonate filtered off, and the resulting solution taken to dryness. The residue in chloroform was shaken with dilute hydrochloric acid to remove the basic portion, and the neutral material gave after crystallisation from ethanol anhydro-*N*-cyanodihydrosecolycorine (IX) (180 mg.), m. p. 215—217°, $[\alpha]_D$ −197° (*c* 0·5 in $CHCl_3$) (Found: C, 64·9; H, 5·8. Calc. for $C_{17}H_{18}O_4N_2$: C, 65·0; H, 5·8%). The mother-liquors from the crystallisation were chromatographed over activated alumina, and the first fraction eluted with benzene–chloroform (1 : 16) gave a further quantity of the anhydrocyano-compound (20 mg.) but the succeeding eluates furnished a solid (25 mg.) which after crystallisation from ethanol yielded *anhydro-*N*-cyano-ω-ethoxydihydrosecolycorine* (III), m. p. 187—188°, $[\alpha]_D$ −174° (*c* 0·7 in $CHCl_3$) (Found: C, 63·2; H, 6·7; OEt, 13·0. $C_{19}H_{24}O_5N_2$ requires C, 63·3; H, 6·7; OEt, 12·5%). This compound did not lose weight on drying *in vacuo* and is probably identical with the " alcoholate of dihydrocyanolycorine anhydride, m. p. 182° " of Kondo and Katsura (1939).

The aqueous acidic solution obtained as above was basified and extracted with chloroform to afford an oil (40 mg.). The combined oily fractions (0·5 g.) from a series of runs were chromatographed over activated alumina and eluted with benzene–chloroform (1 : 16). The first elutate furnished *anhydrodehydrodihydrosecolycorine* (XIII) (15 mg.), m. p. 226° identical with that of a sample prepared from anhydrodihydrosecolycorine (see below). Further elution with the same solvent mixture gave a semicrystalline product (150 mg.) which after drainage on a porous plate was crystallised from ethyl methyl ketone, to give the *imidate* (V), m. p. 110°, which after drying at 105° *in vacuo* rose to 156—158°, $[\alpha]_D$ −89·8° (*c* 0·6 in $CHCl_3$) (Found: C, 63·2; H, 6·6; N, 7·4; OEt, 12·5. $C_{19}H_{24}O_5N_2$ requires C, 63·3; H, 6·7; N, 7·8; OEt, 12·5%). The infrared spectrum showed a strong band at 1608 cm.$^{-1}$ (CN) which should be compared with the band at 1600 cm.$^{-1}$ for *O*-ethyl-*N*-methyl-*N*-phenyl*iso*urea. The imidate (140 mg.) was also obtained as the major product of the action of hot ethanolic potassium hydroxide on anhydro-*N*-cyanodihydrosecolycorine (200 mg.) for 2 hr. Further elution of the above column with acetone gave an oil from which anhydrodihydrosecolycorine (16 mg.) was isolated after crystallisation from ethyl methyl ketone.

Anhydrodihydrosecolycorine (X).—Anhydro-*N*-cyanodihydrosecolycorine (100 mg.) and 30% sulphuric acid (5 ml.) were heated under reflux for 1·5 hr. then diluted with water and extracted with chloroform. The aqueous solution was basified and extracted with chloroform, to yield the anhydro-*seco*-compound, m. p. 198°, $[\alpha]_D$ −181° (*c* 0·5 in $CHCl_3$) (Found: C, 66·5; H, 6·6. Calc. for $C_{16}H_{19}O_4N$: C, 66·4; H, 6·6%). The action of acid on the imidate (V) gave the same product in 60% yield.

Dehydrodihydrosecolycorine (XIII).—Repeated evaporation of a chloroform solution of the above anhydro-*seco*-compound to dryness on a water-bath gave the *dehydro-compound* readily separable from the starting material because of its low solubility in ethyl methyl ketone from which it crystallised with m. p. 226°, $[\alpha]_D$ −81° (*c* 0·3 in $CHCl_3$) (Found: C, 67·1; H, 5·9. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0%). The ultraviolet absorption spectrum showed $\lambda_{max.}$ 320, 290, and 230 mμ (log ε 4·24, 3·62, and 3·62) similar to those of 3 : 4-dihydro*iso*quinolines (Tomita, Uyeo, Sawa, Doi, and Miwa, *J. Pharm. Soc. Japan*, 1949, **69**, 22). Hydrogenation in acetic acid with platinum oxide catalyst regenerated the original anhydro-compound (X).

ω-Ethoxydihydrosecolycorine (IV).—*N*-Cyano-ω-ethoxydihydrosecolycorine (100 mg.) and 30% sulphuric acid (5 ml.) were heated under reflux for 1 hr. The cooled solution was diluted with water and extracted with chloroform to recover unchanged starting material (10m g.), then made alkaline, and the chloroform extract was chromatographed over activated alumina. The first and third eluates were oily and yielded no crystalline material; however the second eluate gave a solid (49 mg.) which furnished pure *ω-ethoxydihydrosecolycorine* (30 mg.),

m. p. 167—168°, $[\alpha]_D$ −168° (*c* 0·5 in $CHCl_3$), after one crystallisation from ethyl methyl ketone (Found: C, 64·1; H, 7·4; N, 4·1; OEt, 13·6. $C_{18}H_{25}O_5N$ requires C, 64·5; H, 7·5; N, 4·2; OEt, 13·4%).

Keto-lactam (XIV).—This was prepared by chromic acid oxidation of anhydro-*N*-cyanodihydro*seco*lycorine (IX) (280 mg.) by Kondo and Katsura's procedure (1939). The crude compound, after three crystallisations from ethanol, furnished the pure *keto-lactam* (28 mg.), m. p. 337° (lit., 341°) (Found: C, 64·2, 63·9; H, 4·6, 4·5. $C_{16}H_{13}O_3N$ requires C, 64·2; H, 4·4%). The ultraviolet absorption spectrum showed $\lambda_{max.}$ in 95% EtOH 246, 266, 332, and 345 mμ (log ε 4·46, 4·35, 4·0, and 4·01) and in 0·001N-ethanolic potassium hydroxide 232, 271, 304, 316, 355, and 370 mμ (log ε 4·10, 4·32, 3·78, 3·79, 4·07, and 4·13). In the infrared there was a strong band with a broad peak at 1667—1650 cm.$^{-1}$ with a medium strength shoulder at 1642 cm.$^{-1}$.

We are indebted to Mr. M. Fukuda and to Mr. T. Takashima for the microanalyses and the ultraviolet absorption measurements respectively. The infrared spectra were taken in part by Mr. S. Okeko, Dainippon Pharmaceutical Co., Osaka, and by Mr. W. Fulmor and his staff, Lederle Laboratories Division, American Cyanamid Co.

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Metal Complexes formed by Some Substituted Phenyldialkyl-phosphines and -arsines.

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A number of complexes of silver(I), copper(I), zinc, cadmium, mercury, cobalt, and nickel halides with *p*-dimethylaminophenyldimethylphosphine and with the corresponding arsine have been prepared and compared with those formed by the unsubstituted ligands and ligands containing *p*-trifluoromethylphenyl groups. In all cases except that of mercury, which has a strong tendency to form d_π–d_π bonds, substitution of a *p*-dimethylamino-group in an arsine $Ph{\cdot}AsMe_2$ increases the stability of complexes, and a *p*-trifluoromethyl group has the reverse effect. With the phosphines, which are stronger donors, this effect is only apparent with zinc and cadmium, which also co-ordinate strongly to nitrogen and oxygen. This suggests that metals which co-ordinate by both a σ and a strong π bond are not appreciably affected by electronic effects which would greatly influence complexes involving only σ or weak π bonds. Several complexes have been prepared in which silver is three co-ordinated.

Electronegativity effects strongly influence the strengths of co-ordinate links. In the absence of any possible double bonding by *d* orbitals these effects are well understood, and may be illustrated by the strong acceptor properties of boron trifluoride relative to trimethylboron. Recently, however, *d* orbitals have been shown to contribute to whole or partial double bonds by forming d_π–p_π bonds (*e.g.*, in sulphates and phosphine oxides, Phillips, Hunter, and Sutton, *J.*, 1945, 146; and in transition-metal complexes with carbon monoxide and cyanides), and by forming d_π–d_π bonds in the complexes of Groups I*b*, II*b*, and VIII with heavier donors of Groups V and VI such as phosphorus, arsenic, or sulphur (Nyholm, *J.*, 1951, 3245; see Chatt, *J.*, 1952, 4300 for references). The overall effect of electronegativity on the stability of complexes in which *d* orbitals are involved is rather complicated as several factors are concerned, *viz.*, (*a*) the normal effect on the σ component of the co-ordinate link, (*b*) the effect on the π component (d_π–d_π bonding), and (*c*) the effect on matching of *d* with *s* and *p* orbitals in cases where dsp^2 or d^2sp^3 σ bonds are involved (see Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332).

The object of the present investigation was to compare the donor properties of some tertiary phosphines and arsines in which strong electronic effects may be transmitted to the phosphorus or arsenic atom without affecting its steric environment. *para*-Substituted

phenyldimethyl(and diethyl)-phosphines and -arsines were selected, since electronic effects are strongly transmitted across a phenyl group, while the electronically active group remains at a distance from the co-ordinate link and does not affect its steric condition. Triarylphosphines were avoided since they tend to give inconveniently insoluble metal complexes in many cases, whereas the aryldialkylphosphines are sufficiently unsymmetrical to result in higher solubilities. The dimethylamino- (electron-repelling) and trifluoromethyl (electron-attracting) groups were used in the eight compounds, $NMe_2 \cdot C_6H_4 \cdot PMe_2$, $C_6H_5 \cdot PMe_2$, $NMe_2 \cdot C_6H_4 \cdot PEt_2$, $C_6H_5 \cdot PEt_2$, $CF_3 \cdot C_6H_4 \cdot PEt_2$, $NMe_2 \cdot C_6H_4 \cdot AsMe_2$, $C_6H_5 \cdot AsMe_2$, $CF_3 \cdot C_6H_4 \cdot AsMe_2$. Unfortunately, attempts to prepare dimethyl-*p*-trifluoromethylphenylphosphine were not successful. In the absence of complications due to *d* orbitals the *p*-dimethylamino-compounds should be stronger donors than the unsubstituted phenyl compounds, owing to the effect: $Me_2N \leftarrow C_6H_4 \rightarrow PR_2$. Similarly the trifluoromethyl-substituted compounds should be weaker donors, $CF_3 \leftarrow C_6H_4 \leftarrow PR_2$. Strong d_π–d_π bonding, however, should be favoured by electronegative substituents.

The evidence about relative stabilities obtained in this work is of an entirely qualitative character; in some instances complexes were obtained and in others no compound could be prepared, some complexes were obviously unstable and very easily decomposed, some smelled strongly of the ligand while others did not. In experiments with nickel complexes, colour changes helped to show how far complex formation had taken place. In view, however, of the large number of experiments carried out, with eight different ligands and eight metals [Cu(I), Ag(I), Au(I), Zn, Cd, Hg, Co, and Ni], the overall result is quite informative. In the first place, attempts were made to prepare complexes between all these metals and dimethylaniline; only an unstable mercuric chloride complex resulted. Since complexes were obtained with phenyldimethylphosphine in all cases, it can be concluded that all these metals co-ordinate to the latter more strongly than to the former, and that co-ordination to the dimethylamino-group is not likely to complicate experiments with the *p*-dimethylaminophenyl series of phosphines and arsines.

Copper, Silver, and Gold.—Numerous tertiary phosphine and arsine complexes of these elements have been described previously, notably by Mann, Purdie, and Wells (*J.*, 1936, 1503; 1937, 1828; 1940, 1209, 1230, 1235) and by Kabesh and Nyholm (*J.*, 1951, 38, 3245; 1952, 1257). These investigations have shown that cuprous but not cupric copper forms complexes with phosphines and arsines, the co-ordination number of the copper being two or more generally four. Silver(I) behaves similarly, the majority of the compounds examined being of the type $[R_3P(\text{or As}) \cdot AgI]_4$ in which the co-ordination number of the silver is four. Gold, on the other hand, forms complexes in both aurous and auric states, and the aurous complexes also differ in normally assuming a covalency of two (*e.g.*, $R_3P \cdot AuI$); however, a covalency of four is apparent in some chelate ditertiary arsine complexes, *e.g.*, [Au(Diarsine)$_2$]X (Nyholm, *Nature*, 1951, **168**, 705).

In the present work few experiments were carried out with gold compounds, but the two compounds isolated, $[(NMe_2 \cdot C_6H_4 \cdot PMe_2)_2Au]I$ and $(Ph \cdot PMe_2)AuI_3$, conform to these rules. Dwyer and Stewart (*J. Proc. Roy. Soc. New South Wales*, 1950, **83**, 177) have described some rather unstable aurous halide complexes of $Ph \cdot AsMe_2$.

The experiments on copper(I) and silver were confined to the iodides, since far more earlier data concern iodides than the other halides, and can be compared with present results.

The effect of the *para*-substituents on the stability of complexes was only noticeable in the case of the arsine series. The arsine $NMe_2 \cdot C_6H_4 \cdot AsMe_2$ afforded a stable complex $(NMe_2 \cdot C_6H_4 \cdot AsMe_2)_2CuI$ with no indication of the formation of a 1 : 1 complex. Burrows and Sandford (*ibid.*, 1936, **69**, 182) described unstable 2 : 1 and 1 : 1 complexes between $Ph \cdot AsMe_2$ and cuprous iodide, and in the present work no $CF_3 \cdot C_6H_4 \cdot AsMe_2$ complex could be isolated at all. Similarly, silver iodide afforded the 2 : 1 complex $(NMe_2 \cdot C_6H_4 \cdot AsMe_2)_2AgI$, which decomposes when its solution in acetone or benzene is warmed, with deposition of silver iodide (which redissolves on cooling). Burrows and Parker (*J. Amer. Chem. Soc.*, 1933, **55**, 4133) failed to obtain a silver iodide complex with

phenyldimethylarsine, and attempts at preparation of such a complex by the present authors also failed, neither could a derivative of $CF_3 \cdot C_6H_4 \cdot AsMe_2$ be prepared. Towards cuprous and silver iodide the donor character of arsenic in the series investigated is in the order $NMe_2 > H > CF_3$. The constitution of the 2 : 1 complexes formed by the amino-arsine $NMe_2 \cdot C_6H_4 \cdot AsMe_2$ is of some interest, since the copper or silver atoms would have the very unusual co-ordination number three if the complexes are monomeric and un-ionised. The cuprous iodide complex $(NMe_2 \cdot C_6H_4 \cdot AsMe_2)_2CuI$ was practically non-conducting in nitrobenzene solution, but its low solubility did not permit reliable measurements of molecular weight. The silver iodide complex was too unstable to investigate, and deposited silver iodide slowly in nitrobenzene solution.

In the phosphine series stable complexes were obtained with all the phosphines studied; phosphorus appears to be a stronger donor than arsenic to all types of acceptor. The most valuable information from this series concerns the possible occurrence of three-co-ordination, since many of the complexes were sufficiently stable to allow molecular-weight and conductivity measurements. The many cuprous and silver iodide complexes with tertiary phosphines previously described are tetrameric 1 : 1 compounds of the type $[PR_3 \cdot Cu(\text{or } Ag)I]_4$. It was therefore surprising that only four complexes of this type were obtained in the present work, *viz.*, $[(Ph \cdot PEt_2)CuI]_{\sim 3}$, $[(CF_3 \cdot C_6H_4 \cdot PEt_2)CuI]_4$, $[(NMe_2 \cdot C_6H_4 \cdot PEt_2)AgI]_4$, and $[(Ph \cdot PEt_2)AgI]_4$. Several other 1 : 1 complexes were prepared, *viz.*, $(NMe_2 \cdot C_6H_4 \cdot PEt_2)CuI$, $(NMe_2 \cdot C_6H_4 \cdot PMe_2)AgI$, and $(Ph \cdot PMe_2)AgI$, but these were either too insoluble to permit molecular-weight measurement (CuI) or were unstable and decomposed rapidly in solution (AgI complexes).

One 3 : 1 complex was obtained, *viz.*, $(CF_3 \cdot C_6H_4 \cdot PEt_2)_2CuI$. This was evidently dissociated in solution in the manner suggested by Nyholm (*J.*, 1952, 1257) for the arsine complexes $(AsMePh_2)_3CuX$, since the measured molecular weight in boiling benzene varied with concentration from 520 to 580, the monomer requiring 892. This complex was virtually non-conducting in nitrobenzene solution. These data are consistent with the equilibria

$$4(CF_3 \cdot C_6H_4 \cdot PEt_2)_3CuI \rightleftharpoons [(CF_3 \cdot C_6H_4 \cdot PEt_2)CuI]_4 + 8CF_3 \cdot C_6H_4 \cdot PEt_2$$

or

$$(CF_3 \cdot C_6H_4 \cdot PEt_2)_3CuI \rightleftharpoons (CF_3 \cdot C_6H_4 \cdot PEt_2)_2CuI + CF_3 \cdot C_6H_4 \cdot PEt_2$$

Six phosphine complexes of the 2 : 1 type were prepared in addition to the two arsine complexes of this type already mentioned. Of these, the cuprous iodide compounds $(NMe_2 \cdot C_6H_4 \cdot PMe_2)_2CuI$ and $(Ph \cdot PMe_2)_2CuI$ are, like $(NMe_2 \cdot C_6H_4 \cdot AsMe_2)_2CuI$, too insoluble for molecular-weight measurements; they are, however, non-electrolytes in nitrobenzene. The silver iodide complexes $(NMe_2 \cdot C_6H_4 \cdot PMe_2)_2AgI$, $(Ph \cdot PMe_2)_2AgI$, $(NMe_2 \cdot C_6H_4 \cdot PEt_2)_2AgI$, and $(CF_3 \cdot C_6H_4 \cdot PEt_2)_2AgI$ are all quite stable and show no signs of decomposition in solution. Nyholm (*loc. cit.*) examined the 2 : 1 complexes of diphenylmethylarsine with cuprous chloride and bromide, and suggested that these were salts $[(R_3As)_4Cu][CuX_2]$ in the solid state, which dissociate in solution giving a mixture of $(AsR_3)_3CuX$ and $(AsR_3 \cdot CuX)_4$. The cuprous chloride complex, $(AsMePh_2)_2CuCl$ (formula weight 587), had a molecular weight 626 (1·79% solution in nitrobenzene) and 758 (2·84% solution). Such a variation with concentration is consistent with an equilibrium between several species.

The four 2 : 1 phosphine–silver iodide complexes, mentioned above, can be crystallised from organic solvents in the normal way, unlike the arsine–cuprous iodide complexes studied by Nyholm. Their molecular weights (boiling benzene) and conductances (10^{-3} molal in nitrobenzene at 25°) are given in Table 1 and indicate that the compounds are monomeric and un-ionised in (benzene) solution. Compounds which do not ionise significantly in nitrobenzene would ionise even less in benzene on account of its lower dielectric constant. This was confirmed in several instances. The absence of any significant change of molecular weight with concentration suggests the absence of dissociation equilibria of the type which probably obtains in the case of Nyholm's arsine–cuprous iodide complexes. Further, some of the 1 : 1 complexes which would be involved in such equilibria have been prepared but immediately decompose in dilute benzene solution and, moreover, solutions of the 2 : 1 complexes do not smell of the phosphines (a fairly sensitive test in view of the very strong smells of the phosphines concerned). The presence

of complexes involving $(AgI_2)^-$ ions is most improbable since no silver iodide is precipitated on addition of an acetone solution of silver nitrate.

TABLE 1. 2 : 1 *Phosphine–silver iodide complexes.*

Formula	M. p.	Formula weight	Λ_m in $PhNO_2$		*M* in C_6H_6				
$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2AgI$	177—178°	597	2·34	*M*	585	579	610	613	
				Wt. %	0·55	0·94	1·30	1·71	
$(Ph{\cdot}PMe_2)_2AgI$	114—115	511	0·93	*M*	568	560	545	515	
				Wt. %	0·56	1·20	1·80	2·45	
$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2AgI$	127—128	653	0·8	*M*	539	561	564	564	554
				Wt. %	0·79	0·94	1·1	1·25	1·7
$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)_2AgI$ ...	94·5—95·5	703	0·4	*M*	710	715	667	682	
				Wt. %	0·69	1·6	2·45	3·15	

Although these results indicate a monomeric structure for the complexes in solution, with the silver exercising the co-ordination number three, they give no information about the structures of the solids. Only one of the phosphines, $(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)$, afforded both types of complex (the tetrameric 1 : 1 and monomeric 2 : 1) with solubilities and stabilities adequate for molecular-weight measurement. The three-co-ordinated thiourea–silver complex has recently been investigated electrometrically (Fyfe, *J.*, 1955, 1032; see also Ahrland and Chatt, *Chem. and Ind.*, 1955, 96).

Zinc, Cadmium, and Mercury.—The tendency of these elements to co-ordinate to nitrogen and oxygen diminishes very markedly from zinc to mercury, and the tendency to co-ordinate to the phosphorus, arsenic, sulphur type of donor *increases* from zinc to mercury. It was therefore noteworthy that, in the present work, the effects of electronically active substituents were clearly evident in the case of zinc, less so for cadmium, and scarcely apparent in the case of mercury.

All the zinc complexes isolated were of the 2 : 1 type, *e.g.*, $(Ph{\cdot}PMe_2)_2ZnI_2$. The compounds $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2ZnX_2$ (X = Cl, Br, or I) could readily be crystallised unchanged, whereas $(Ph{\cdot}PMe_2)_2ZnI_2$ and $(Ph{\cdot}PEt_2)_2ZnI_2$ decomposed easily and smelled of the phosphine (no chlorides or bromides of this type could be prepared), and no trifluoromethyl derivative could be obtained. The arsine series was similar, and no derivative of $CF_3{\cdot}C_6H_4{\cdot}AsMe_2$ could be obtained. As expected, all the zinc complexes were decomposed by 2 : 2′-dipyridyl, with liberation of the free phosphine or arsine.

A large number of cadmium complexes was prepared, and both 1 : 1 and 2 : 1 types were formed. No derivative of $CF_3{\cdot}C_6H_4{\cdot}AsMe_2$ could be isolated, but the phosphine $CF_3{\cdot}C_6H_4{\cdot}PEt_2$ afforded the complex $(CF_3{\cdot}C_6H_4{\cdot}PEt_2)CdI_2$. That cadmium resembles zinc in the effects of the *para*-substituents also appeared from the observation that, whereas both $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdI_2$ and $(Ph{\cdot}PMe_2)CdI_2$ are decomposed by 2 : 2′-dipyridyl, yet the former is unaffected by *p*-toluidine while the latter is decomposed with liberation of phenyldimethylphosphine. The 1 : 1 complexes are often only slightly soluble (particularly chlorides and bromides), so readily separate from solution. The only 2 : 1 complexes that could be isolated were derived from the apparently stronger donors, $NMe_2{\cdot}C_6H_4{\cdot}PMe_2$, $NMe_2{\cdot}C_6H_4{\cdot}PEt_2$, $Ph{\cdot}PEt_2$, and $NMe_2{\cdot}C_6H_4{\cdot}AsMe_2$; iodides were easier to obtain than the bromides and chlorides.

Numerous 1 : 1 cadmium halide complexes with phosphines and arsines have previously been described, and have been assumed to have a halogen-bridged dimeric structure $R_3P(X)CdX_2Cd(X)PR_3$. The 1 : 1 cadmium chloride and bromide complexes were not sufficiently soluble to permit molecular-weight measurement, but the iodide $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdI_2$ was studied in several solvents. The analogous 1 : 1 diethyl compound rather surprisingly could not be prepared. The 1 : 1 complex $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdI_2$ was almost non-conducting in nitrobenzene and only slightly conducting in acetone (molal conductances 1 and 5 respectively at 10^{-3}; compare cadmium iodide, 790 at 10^{-3}m in acetone). The molecular weight of this complex, measured ebullioscopically, varied with solvent and concentration, but was generally within the range 500—1000 corresponding to a monomer (*M*, 547)–dimer equilibrium. Except in ethanol, in which the complex was monomeric (observed molecular weights from 482 to

569), the degree of association increased with concentration, and association to the dimer was favoured by non-polar solvents. For example, the observed degree of association was 1·0—1·2 in acetone, 1·5—1·8 in chloroform, and 1·5—2·0 in benzene. Although interaction with alcohol or acetone to give four-co-ordinate complexes is possible, this could not occur in chloroform or benzene. In nitrobenzene (cryoscopically) the complex was monomeric, with some apparent dissociation at the lower concentrations; there was evidently some interaction with the solvent since the solutions were deep orange. Since the monomeric form of the complex, whether bonded to solvent molecules or not, is likely to be more polar than the bridged dimeric form, association to the dimer should, as observed, be favoured by low polarity of solvent. The trifluoromethyl complex $(CF_3 \cdot C_6H_4 \cdot PEt_2)CdI_2$ behaved in a similar way; dimeric in benzene, it was only slightly associated in acetone in which its molal conductance was only 1·3 at 10^{-3}M (25°). The 1 : 1 tri-*n*-propylphosphine complex $n\text{-}Pr_3P,CdI_2$, one of many described by Evans, Mann, Peiser, and Purdie (*J.*, 1940, 1208), was re-examined and found to be monomeric in acetone, but dimeric in benzene and chloroform. This behaviour may very well be due to co-ordination with acetone.*

Mercury co-ordinates very strongly with donors of the phosphine and arsine type, capable of d_π bonding, and among the many complexes prepared in the present work there was none which suggested that *para*-substitution of trifluoromethyl for hydrogen reduced the stability of a complex. All the mercury complexes prepared were odourless and readily recrystallised from solvents in the absence of any added phosphine or arsine. Both 1 : 1 and 2 : 1 complexes were prepared. The former resemble their cadmium analogues in respect of solubility, but several were sufficiently soluble to allow molecular-weight measurement. The complex $(Ph \cdot PEt_2)HgBr_2$ was dimeric in benzene, but the degree of association in acetone varied from 1·2 to 1·6. Similarly, the complex $(CF_3 \cdot C_6H_4 \cdot PEt_2)HgBr_2$, dimeric in benzene, was partly associated in acetone (1·4—1·7). The tri-*n*-propylphosphine complexes $Pr^n{}_3P,HgBr_2$ and $Pr^n{}_3P,HgI_2$ (Mann *et al.*, *loc. cit.*) were also only partly associated to the dimers in boiling acetone, the observed degrees of association being 1·5—1·85 and 1·2—1·7, respectively.

The compound $(NMe_2 \cdot C_6H_4 \cdot PMe_2)_2HgI_2$ reacts with two mols. of methyl iodide in acetone solution at room temperature. The product is a *P*-methiodide since the same substance was formed from the phosphine methiodide and potassium mercuri-iodide, and a similar dimethiodide was obtained from $(Ph \cdot PMe_2)_2HgI_2$ in which there are no dimethylamino-groups in the ligand. Several phosphonium and arsonium mercuri-iodides have been prepared and are described in the Experimental section; their molal conductances in nitrobenzene at 25° are all about 60—70. The cadmium complexes did not react with methyl iodide directly, but the phosphonium and arsonium cadmi-iodides were readily obtained from the quarternary iodides and cadmium iodide in ethanol.

Cobalt and Nickel.—Only the phosphine $NMe_2 \cdot C_6H_4 \cdot PMe_2$ afforded isolable complexes with cobalt(II) chloride and bromide, and these were difficult to purify. No cobalt arsine complexes could be obtained with the ligands investigated.

All the phosphines studied formed red 2 : 1 complexes with nickel, of the type $(R_2P)_2NiX_2$ (X = Cl, Br, I). Of the arsines, however, only $NMe_2 \cdot C_6H_4 \cdot AsMe_2$ afforded isolable complexes, $(NMe_2 \cdot C_6H_4 \cdot AsMe_2)_2NiBr_2$ and the iodide. Since the reactants are colourless or green and the complexes are red or brown-red, colour changes provided useful qualitative information about relative stabilities. Thus, addition of $NMe_2 \cdot C_6H_4 \cdot AsMe_2$ to a green ethanolic solution of nickel chloride caused no colour change, though the bromide and iodide gave deep red solutions from which the solid complexes could be isolated. Similarly, addition of the same quantity of $Ph \cdot AsMe_2$ to equimolar amounts of the three halides in equal volumes of ethanol caused a colour change only with nickel iodide, and the arsine $CF_3 \cdot C_6H_4 \cdot AsMe_2$ produced a faint brown colour only with the iodide. Consequently, the stability order in co-ordination with these arsines is I > Br > Cl but this apparent order may well be determined by variations in the solvation energies of the three halide ions.* Addition of $NMe_2 \cdot C_6H_4 \cdot AsMe_2$ to ethanolic nickel iodide results in a deep red colour

* The authors are indebted to a Referee for this point.

and the solid complex can be separated, while Ph·$AsMe_2$ produces a brown colour and no product can be isolated, and CF_3·C_6H_4·$AsMe_2$ causes only a very pale brown colour. Hence it is safe to conclude that the order of donor strength to nickel iodide is NMe_2·C_6H_4·$AsMe_2$ > Ph·$AsMe_2$ > CF_3·C_6H_4·$AsMe_2$.

Experimental

Preparation of Ligands.—The phosphines Ph·PMe_2, Ph·PEt_2, NMe_2·C_6H_4·PMe_2, and NMe_2·C_6H_4·PEt_2 were prepared as previously described, by the action of methyl- or ethylmagnesium halide on the dichlorophosphine, except that separation of the reaction product (after hydrolysis) by steam-distillation was found to be better than other methods described.

Diethyl-p-*trifluoromethylphenylphosphine.*—*p*-Bromobenzotrifluoride (76·4 g.) was added slowly to magnesium (8·3 g.) in dry ether (500 c.c.). Diethylchlorophosphine (Beeby and Mann, *J.*, 1951, 411) (43·2 g.) in ether (100 c.c.) was added to the resulting Grignard solution during 40 min. The mixture was then refluxed for ½ hr. and hydrolysed with water (60 c.c.) followed by 6N-sodium hydroxide (150 c.c.). The phosphine was separated by steam-distillation (N_2 atmosphere), after previous removal of most of the ether, extracted with ether, dried, and distilled under nitrogen. The *phosphine*, b. p. 106—108°/13 mm. (26 g., 33%), which oxidises in the air more easily than the others prepared, was distributed in a number of sealed tubes under nitrogen (Found: F, 24·7. $C_{11}H_{14}F_3P$ requires F, 24·4%).

For characterisation the phosphine was added to methyl iodide (excess) in benzene, and the *methiodide* separated as an oil which crystallised slowly; recrystallised from ethanol, it had m. p. 108—109° (Found: I, 33·5. $C_{12}H_{17}F_3PI$ requires I, 33·8%).

p-*Dimethylaminophenyldimethylarsine.*—*p*-Bromodimethylaniline (14·5 g.) in dry ether (20 c.c.) was slowly added to lithium (1·0 g.) in dry ether (40 c.c.) under a nitrogen atmosphere. When reaction was finished, cacodyl iodide (8·0 g.) in ether (20 c.c.) was slowly added. The mixture was refluxed for 1 hr. and then hydrolysed. The arsine was extracted with ether, dried ($MgSO_4$), and separated by distillation, which yielded dimethylaniline (2 c.c.) followed by the arsine, b. p. 147—150°/82 mm. (5·5 g., 70%). For characterisation the arsine was added to methyl iodide (excess) in ether; the *methiodide* which separated was crystallised from ethanol, and formed colourless plates, m. p. 259—260° (decomp.) (Found: C, 35·9; H, 5·0. $C_{11}H_{19}NIAs$ requires C, 35·95; H, 5·2%).

Phenyldimethylarsine was prepared as previously described.

Dimethyl-p-*trifluoromethylphenylarsine.*—This was prepared from *p*-trifluoromethylphenylmagnesium bromide and cacodyl iodide by a method similar to that used to prepare diethyl-*p*-trifluoromethylphenylphosphine, and was obtained in 75% yield, as a pale yellow oil, b. p. 202—204°. The *methiodide* formed colourless needles (from ethanol), m. p. 168° (Found: C, 30·0; H, 3·5; I, 32·3. $C_{10}H_{10}F_3IAs$ requires C, 30·6; H, 3·35; I, 32·4%).

Since carbon and hydrogen analyses of compounds containing fluorine often gave erratic results, such compounds were generally analysed by determination of metal and halogen. Molecular weights were determined ebullioscopically, unless otherwise stated, in a Swietoslawski apparatus, two thermistors being used to measure temperature differences. Molal conductances are for 10^{-3}m-solutions in nitrobenzene at 25°.

Copper and silver complexes were prepared by addition of a concentrated ethanolic solution of the ligand (1 mol.) to cuprous or silver iodide (1 mol.) dissolved in concentrated aqueous potassium iodide. The mixture was shaken, and the complex separated and crystallised from a suitable solvent.

Complexes of zinc, cadmium, mercury, cobalt, and nickel were prepared by addition of an ethanolic solution of the ligand to an ethanolic solution of the appropriate metal halide. Complexes of mercuric iodide were prepared by dissolving the solid iodide in an ethanolic or acetone solution of the ligand, or by addition of an ethanolic solution of the ligand to aqueous potassium mercuri-iodide. The *complexes* listed in Table 2 were prepared by these methods, except those whose preparation is described below.

Tris-(p-*dimethylaminophenyldiethylphosphine*)*monoiodocopper.*—Cuprous iodide (1 mol.) was dissolved in a solution of the phosphine (NMe_2·C_6H_4·PEt_2) (16 mols.) in ethanol. The *complex* which separated was crystallised from ethanol–benzene (1 : 1) and formed large colourless crystals, m. p. 89—91° (Found: C, 51·4; H, 7·0; N, 5·1. $C_{36}H_{60}N_3IP_3Cu$ requires C, 52·7; H, 7·3; N, 5·1%).

Tris(*diethyl*-p-*trifluoromethylphenylphosphine*)*monoiodocopper.*—This *complex* separated when the phosphine (CF_3·C_6H_4·PEt_2) (6 mols.) was shaken with a solution of cuprous iodide

TABLE 2.

Complex number	Substance	M. p.*	Found (%) C	Found (%) H	Formula	Reqd. (%) C	Reqd. (%) H
I	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2CuI$	156—157°[a]	42·4	5·0	$C_{20}H_{32}N_2IP_2Cu$	42·2	5·8
II	$(Ph{\cdot}PMe_2)_2CuI$	98·5—99[c]	41·1	4·4	$C_{16}H_{22}IP_2Cu$	41·3	4·7
III	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2CuI$	210—212[c]	36·4	4·85	$C_{12}H_{20}NIPCu$[g]	36·0	5·0
IV	$(Ph{\cdot}PEt_2)CuI$	153·5—155[a]	33·8	4·4	$C_{10}H_{15}IPCu$	33·6	4·2
V	$[(CF_3{\cdot}C_6H_4{\cdot}PEt_2)CuI]_4$	165—166[a]	—	—	$C_{44}H_{56}F_{12}I_4P_4Cu_4$[h]	—	—
VI	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2CuI$	135—136[c]	37·8	4·9	$C_{20}H_{32}N_2IAs_2Cu$	37·5	5·0
VII	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2AgI$	177—178[c]	39·7	5·0	$C_{20}H_{32}N_2IP_2Ag$	40·1	5·3
VIII	$(Ph{\cdot}PMe_2)_2AgI$	114—115[c]	37·4	4·4	$C_{16}H_{22}IP_2Ag$	37·5	4·3
IX	$[(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)AgI]_4$	203—205[b]	32·5	4·3	$C_{44}H_{80}N_4I_4P_4Ag_4$[i]	32·4	4·5
X	$[(Ph{\cdot}PEt_2)AgI]_4$	138—139[c]	30·2	4·05	$C_{40}H_{60}I_4P_4Ag_4$[j]	29·9	3·7
XI	$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)_2AgI$	94·5—95·5[a]	—	—	$C_{22}H_{30}F_6IP_2Ag$[k]	—	—
XII	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2AgI$	146—148[c]	34·5	4·6	$C_{20}H_{32}N_2IAs_2Ag$	34·8	4·6
XIII	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2ZnCl_2$	151·5—152[a]	48·4	6·8	$C_{20}H_{32}N_2Cl_2P_2Zn$	48·1	6·4
XIV	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2ZnBr_2$	146[a]	40·6	5·4	$C_{20}H_{32}N_2Br_2P_2Zn$	40·8	5·4
XV	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2ZnI_2$	159—160[a]	35·2	4·7	$C_{20}H_{32}N_2I_2P_2Zn$	35·3	4·7
XVI	$(Ph{\cdot}PMe_2)_2ZnI_2$	135[a]	32·1	3·7	$C_{16}H_{22}I_2P_2Zn$	32·1	3·7
XVII	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2ZnI_2$	115—117[a]	38·8	5·6	$C_{24}H_{40}N_2I_2P_2Zn$[l]	39·1	5·4
XVIII	$(Ph{\cdot}PEt_2)_2ZnI_2$	172·5—174[a]	36·8	5·0	$C_{20}H_{32}I_2P_2Zn$	36·8	4·6
XIX	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2ZnI_2$	118[a]	30·8	4·0	$C_{20}H_{32}N_2I_2As_2Zn$	31·2	4·2
XX	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdCl_2$	215—217[f]	32·7	4·4	$C_{10}H_{16}NCl_2PCd$	32·9	4·4
XXI	$(Ph{\cdot}PMe_2)CdCl_2$	302—304[a,e]	29·6	3·4	$C_8H_{10}Cl_2PCd$	29·9	3·1
XXII	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)CdCl_2$	180[a,e]	29·4	3·9	$C_{10}H_{16}NCl_2AsCd$[m]	29·2	4·05
XXIII	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdBr_2$	221—222[f]	26·7	3·2	$C_{10}H_{16}NBr_2PCd$	26·5	3·5
XXIV	$(Ph{\cdot}PMe_2)CdBr_2$	~180[a,e]	23·4	2·7	$C_8H_{10}Br_2PCd$	23·4	2·7
XXV	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)CdBr_2$	210—212[a]	24·45	3·5	$C_{10}H_{16}NBr_2AsCd$[n]	24·2	3·2
XXVI	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)CdI_2$	144—145[a]	21·9	2·8	$C_{10}H_{16}NI_2PCd$	21·9	2·9
XXVII	$(Ph{\cdot}PMe_2)CdI_2$	75[d]	19·7	2·2	$C_8H_{11}I_2PCd$	19·1	2·2
XXVIII	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2CdI_2$	116—118[a]	37·1	4·8	$C_{28}H_{40}N_2I_2P_2Cd$[o]	36·8	5·1
XXIX	$(Ph{\cdot}PEt_2)_2CdI_2$	102—103[a]	—	—	$C_{20}H_{32}I_2PCd$[p]	—	—
XXX	$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)CdI_2$	123·5—124·5[a]	—	—	$C_{11}H_{14}F_3I_2PCd$[q]	—	—
XXXI	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2CdI_2$	116[a]	29·8	4·2	$C_{20}H_{32}N_2I_2As_2Cd$	29·4	3·9
XXXII	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)HgCl_2$	233—235[b,e]	26·8	4·0	$C_{10}H_{16}NCl_2Hg$	26·6	3·5
XXXIII	$(Ph{\cdot}PMe_2)HgCl_2$	168—169[f]	23·2	2·5	$C_9H_{11}Cl_2PHg$	23·4	2·7
XXXIV	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)HgCl_2$	199[b,e]	24·4	3·1	$C_{10}H_{16}NCl_2AsHg$[r]	24·2	3·2
XXXV	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)HgBr_2$	201—204[b]	22·6	3·1	$C_{10}H_{16}NBr_2PHg$	22·2	3·0
XXXVI	$(Ph{\cdot}PMe_2)HgBr_2$	133—135[b]	19·4	2·2	$C_9H_{11}Br_2PHg$	19·3	2·2
XXXVII	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)HgBr_2$	170·5—173[b]	26·0	3·7	$C_{18}H_{30}NBr_2PHg$[s]	25·3	3·5
XXXVIII	$(Ph{\cdot}PEt_2)HgBr_2$	120—121[c]	23·2	2·8	$C_{10}H_{15}Br_2PHg$	22·8	2·8
XXXIX	$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)HgBr_2$	116·5—117·5[a]	—	—	$C_{11}H_{14}F_3Br_2PHg$[t]	—	—
XL	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)HgBr_2$	171[b,e]	20·8	2·7	$C_{10}H_{16}NBr_2AsHg$	20·6	2·7
XLI	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2HgI_2$	170—171[b]	29·2	3·9	$C_{20}H_{32}N_2I_2P_2Hg$	29·4	3·9
XLII	$(Ph{\cdot}PMe_2)_2HgI_2$	115—117[c]	26·6	3·2	$C_{16}H_{22}I_2P_2Hg$	26·2	3·0
XLIII	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2HgI_2$	157—159[a]	32·8	4·7	$C_{24}H_{40}N_2I_2P_2Hg$	33·0	4·6
XLIV	$(Ph{\cdot}PEt_2)_2HgI_2$	130—131[a]	30·9	3·8	$C_{20}H_{30}I_2P_2Hg$	30·5	3·8
XLV	$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)HgI_2$	130·5—132[a]	—	—	$C_{11}H_{14}F_3I_2PHg$[u]	—	—
XLVI	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2NiCl_2$	205·5[c]	48·6	6·3	$C_{20}H_{32}N_2Cl_2P_2Ni$	48·8	6·5
XLVII	$(Ph{\cdot}PMe_2)_2NiCl_2$	152·5—153[a]	47·4	5·6	$C_{16}H_{22}Cl_2P_2Ni$	47·3	5·4
XLVIII	$(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)_2NiCl_2$	110—111[a]	52·8	7·7	$C_{24}H_{40}N_2Cl_2P_2Ni$[v]	52·5	7·3
XLIX	$(CF_3{\cdot}C_6H_4{\cdot}PEt_2)_2NiCl_2$	137·5—139·5[a]	—	—	$C_{22}H_{30}F_6Cl_2P_2Ni$[w]	—	—
L	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2NiBr_2$	179—181[c,e]	41·5	5·8	$C_{20}H_{32}N_2Br_2P_2Ni$	41·6	5·5
LI	$(Ph{\cdot}PMe_2)_2NiBr_2$	137·5—138·5[a]	39·2	4·8	$C_{16}H_{22}Br_2P_2Ni$	38·9	4·5
LII	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2NiBr_2$	183—184[a]	36·1	4·5	$C_{20}H_{32}N_2Br_2As_2Ni$	35·9	4·8
LIII	$(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2NiI_2$	173—175[a]	35·6	4·8	$C_{20}H_{32}N_2I_2P_2Ni$	35·5	4·7
LIV	$(NMe_2{\cdot}C_6H_4{\cdot}AsMe_2)_2NiI_2$	175—177[a]	31·6	4·3	$C_{20}H_{32}N_2I_2As_2Ni$	31·5	4·2

* Denotes with decomposition.

Molal conductances: (III), 0·72; (IV), 2·58; (VI), 1·32. Crystallised from [a] ethanol, [b] acetone, [c] benzene, [d] chloroform, [e] ethanol–acetone. [f] Insoluble in common solvents, washed with much hot ethanol. [g] Found: N, 3·1. Reqd.: N, 3·5%. [h] Found: Cu, 15·0; I, 30·0%; *M*, 1600. Reqd.: Cu, 14·95; I, 29·9%; *M*, 1698. [i] Found: *M*, 1590, 1664. Reqd.: *M*, 1776. [j] Found: AgI, 58·5%; *M*, 1460, 1640, 1785. Reqd.: AgI, 58·4%; *M*, 1604. [k] Found: AgI, 33·4. Reqd.: 33·4%. [l] Found: N, 3·4%; *M*, 680, 684. Reqd.: N, 3·8%; *M*, 737. [m] Found: N, 3·4. Reqd.: N, 3·4%. [n] Found: N, 2·7. Reqd.: N, 2·8%. [o] Found: *M*, 763, 745. Reqd.: *M*, 784. [p] Found: Cd, 16·1%; *M*, 688, 710. Reqd.: Cd, 16·1%; *M*, 698. [q] Found: Cd, 18·7; I, 41·9. Reqd.: Cd, 18·8; I, 42·2%. [r] Found: N, 3·1. Reqd.: N, 2·8%. [s] Found: N, 2·5; Br, 28·4. Reqd.: N, 2·5; Br, 28·1%. [t] Found: Br, 26·8. Reqd.: Br, 26·9%. [u] Found: I, 36·7. Reqd.: I, 36·8%. [v] Found: N, 4·6%; *M*, 528, 522, 602, 550. Reqd.: N, 5·1%; *M*, 548. [w] Found: Ni, 9·65; Cl, 12·1. Reqd.: Ni, 9·8; Cl, 11·9%.

(1 mol.) in concentrated aqueous potassium iodide, and crystallised from ethanol as colourless needles, m. p. 94—95° [Found: Cu, 7·1; I, 14·4%; *M*, 525 (0·20% solution in benzene), 555 (0·43%), 548 (0·70%), 577 (0·96%) 582 (1·35%). $C_{33}H_{43}F_9IP_3Cu$ requires Cu, 7·1; I, 14·2%; *M*, 892·5].

p-Dimethylaminophenyldimethylphosphineiodosilver.—A suspension of silver iodide (0·3 g., 1·3 mols.) in a solution of the 2 : 1 complex $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2AgI$ (0·59 g., 1 mol.) in benzene (15 c.c.) was boiled under reflux for 5 hr. During this time small crystals separated and adhered to the side of the flask; they were washed from unchanged silver iodide by light petroleum. The mixture was filtered, and colourless crystals were deposited from the cold filtrate. Both crops of crystals (0·6 g.) had the same m. p. and mixed m. p. (204—205°). Attempts at recrystallisation or dissolution for molecular-weight measurement caused decomposition to silver iodide and the 2 : 1 compound $(NMe_2{\cdot}C_6H_4{\cdot}PMe_2)_2AgI$ (Found: C, 29·2; H, 3·9. $C_{10}H_{16}NIPAg$ requires C, 28·9; H, 4·2%). The complex $(Ph{\cdot}PMe_2)AgI$ was prepared in a similar way, but could not be obtained pure; it had m. p. 80·5—83° (Found: C, 26·4; H, 3·1. Calc. for $C_8H_{11}IPAg$: C, 25·7; H, 3·4%). Dissolution in an organic solvent resulted in decomposition to silver iodide and $(Ph{\cdot}PMe_2)_2AgI$.

Bis-(p-dimethylaminophenyldiethylphosphine)monoiodosilver.—The diethylphosphine $(NMe_2{\cdot}C_6H_4{\cdot}PEt_2)$ (4 mols.) was shaken with a solution of silver iodide (1 mol.) in concentrated aqueous potassium iodide. The white *complex* which separated was crystallised from acetone, and formed colourless rhombs, m. p. 127—128° (Found: C, 44·0; H, 6·3; N, 4·6. $C_{24}H_{40}N_2IP_2Ag$ requires C, 44·1; H, 6·1; N, 4·3%). The molal conductance in nitrobenzene and the molecular weight are given in Table 1.

Bis-(p-dimethylaminophenyldimethylphosphine)monoiodogold.—The dimethylphosphine $NMe_2{\cdot}C_6H_4{\cdot}PMe_2$ (0·1 g.) in ethanol (6 c.c.) was slowly added to a solution of potassium auri-iodide (0·2 g.) in ethanol (10 c.c.). After the first portion of the phosphine had been added the brown solution became colourless. When the addition was complete the solution was concentrated to 5 c.c. by boiling. The pale cream crystals which separated from the cold solution were crystallised from benzene; they had m. p. 198—199°, molal conductance 12·5 (Found: C, 34·8; H, 4·4. $C_{20}H_{32}N_2IP_2Au$ requires C, 35·0; H, 4·4%).

Phenyldimethylphosphinetri-iodogold.—Phenyldimethylphosphine dissolved in 6 vols. of ethanol was added to a solution of potassium auri-iodide (0·1 g.) in ethanol containing a trace of iodine until the solution became colourless. When the solution was concentrated to 10 c.c. and set aside for several hours colourless lustrous plates separated (0·4 g.) and were recrystallised from ethanol; they had m. p. 142° (slight decomp.) (Found: C, 13·7; H, 1·6. $C_8H_{11}I_3PAu$ requires C, 13·4; H, 1·5%). When pure potassium auri-iodide free from iodine was used a yellow oil separated, which could not be induced to crystallise.

Bis-(p-dimethylaminophenyldimethylphosphine)dichlorocadmium.—The complex (XX) (1 mol.) was dissolved in a solution of the phosphine $NMe_2{\cdot}C_6H_4{\cdot}PMe_2$ (2 mols., 100% excess) in acetone, and the cooled solution deposited the 2 : 1 *complex* as large colourless plates, m. p. 138—139° (Found: C, 43·8; H, 6·1; N, 5·25. $C_{20}H_{32}N_2Cl_2P_2Cd$ requires C, 44·0; H, 5·9; N, 5·14%).

Bis-(p-dimethylaminophenyldimethylphosphine)dibromocadmium.—This was prepared similarly, from (XXIII), and separated from acetone as large rhombohedral crystals, m. p. 154—155° (Found: C, 37·7; H, 5·05; N, 4·30. $C_{20}H_{32}N_2Br_2P_2Cd$ requires C, 37·8; H, 5·05; N, 4·42%).

Bis-(p-dimethylaminophenyldimethylarsine)dibromocadmium.—This was prepared similarly, from (XXV), and formed colourless crystals (from acetone), decomp. 230° with previous softening at 100° (Found: C, 33·5; H, 4·45; N, 3·6. $C_{20}H_{32}N_2Br_2As_2Cd$ requires C, 33·2; H, 4·43; N, 3·9%).

Reaction of Zinc and Cadmium Complexes with 2 : 2′-Dipyridyl and with p-Toluidine.—2 : 2′-Dipyridyl (0·08 g.) in ethanol (10 c.c.) was added to a solution of the complex (XV) (0·34 g.) in ethanol. A white crystalline precipitate of dipyridyldi-iodozinc, m. p. ~370°, was formed when the solution was heated to boiling, and was removed by filtration (Found: N, 6·1. Calc. for $C_{10}H_8N_2I_2Zn$: N, 5·9%). The filtrate was concentrated to about 2 c.c. and a solution of methyl iodide (1 c.c.) in ether (20 c.c.) was added; the resulting white precipitate was identified as *p*-dimethylaminophenyltrimethylphosphonium iodide by m. p. and mixed m. p., both 264—265°.

When 2 : 2′-dipyridyl (0·1 g.) in ethanol (5 c.c.) was added to a solution of the complex (XXVI) (0·11 g.) in ethanol (25 c.c.), the white precipitate which formed immediately was collected and identified as dipyridyldi-iodocadmium by m. p. 354—356°, mixed m. p. 356—358°. The filtrate smelled strongly of the liberated phosphine, which was identified (as above) as the methiodide.

No detectable odour of the free phosphine resulted when the same complex was boiled under reflux with *p*-toluidine in excess.

2 : 2′-Dipyridyldi-iodocadmium was precipitated immediately in the cold when 2 : 2′-dipyridyl in ethanol was added to an ethanol solution of the compound (XXVII), and phenyldimethylphosphine was identified in the filtrate by precipitation as methiodide. This phosphine was also displaced from the same complex by *p*-toluidine, with formation of *di-p-toluidinedi-iodocadmium*, m. p. 179—180° (from ethanol) (Found : C, 28·3; H, 2·9. $C_{14}H_{18}N_2I_2Cd$ requires C, 28·1; H, 3·1%).

Bis-(p-*dimethylaminophenyldimethylarsine*)*dichloromercury*.—This *complex* crystallises in large colourless plates when a hot acetone solution of the 1 : 1 complex, to which excess of the arsine has been added, is cooled; it has m. p. 137·5—138·5° (Found : C, 33·4; H, 4·4; N, 4·25. $C_{20}H_{32}N_2Cl_2As_2Hg$ requires C, 33·2; H, 4·4; N, 3·9%). The *dibromo-complex*, prepared similarly, has m. p. 140—141·5° (from acetone) (Found : C, 29·6; H, 4·0. $C_{20}H_{32}N_2Br_2As_2Hg$ requires C, 29·6; H, 4·0%).

Reaction between Bis-(p-*dimethylaminophenyldimethylphosphine*)*mercuric Iodide and Methyl Iodide*.—Methyl iodide (2·8 g.) in acetone (10 c.c.) was added to a solution of the complex (XLI) (1 g.) in acetone (20 c.c.). Pale yellow crystals (0·44 g.) of *bis-*(p-*dimethylaminophenyltrimethylphosphonium*)*mercuri-iodide* separated during 2 hr. at room temperature, and were crystallised from acetone (m. p. 171—172°) (Found : C, 23·9; H, 3·7. $C_{22}H_{38}N_2I_4P_2Hg$ requires C, 24·0; H, 3·7%). The molal conductance was 72·7.

Bis(*trimethylphenylphosphonium*) *mercuri-iodide* was prepared similarly, from the complex (XLII), and afforded pale yellow crystals (from acetone), m. p. 187—188° (Found : C, 20·3; H, 2·8. $C_{18}H_{26}I_4P_2Hg$ requires C, 20·6; H, 2·7%). The molal conductance was 69·0.

These mercuri-iodides, and others listed below together with some cadmi-iodides, were also prepared by addition of the appropriate quaternary iodide in ethanol to aqueous-alcoholic potassium mercuri-iodide, or to ethanolic cadmium iodide. The mercuri-iodides were all pale yellow and the cadmi-iodides colourless.

Bis(*trimethylphenylammonium*) *mercuri-iodide* (from ethanol), m. p. 186°, molal conductance 67·6 (Found : C, 22·2; H, 2·9. $C_{18}H_{32}N_2I_4Hg$ requires C, 22·0; H, 3·2%). *Bis*(*trimethylphenylarsonium*) *mercuri-iodide* (from ethanol), m. p. 192°, molal conductance 67·3 (Found : C, 19·2; H, 2·2. $C_{18}H_{28}I_4As_2Hg$ requires C, 19·5; H, 2·5%). *Bis-*(p-*dimethylaminophenyltrimethylarsonium*) *mercuri-iodide* (from ethanol), m. p. 164°, molal conductance 72·7 (Found : C, 21·9; H, 3·35. $C_{22}H_{38}N_2I_4As_2Hg$ requires C, 22·2; H, 3·2%). *Bis*(*trimethylphenylammonium*) *cadmi-iodide* (from ethanol), m. p. 195° (Found : C, 24·4; H, 3·1. $C_{18}H_{32}N_2I_4Cd$ requires C, 24·2; H, 3·1%). *Bis*(*trimethylphenylphosphonium*) *cadmi-iodide* (from ethanol), m. p. 190° (Found : C, 23·3; H, 3·2. $C_{18}H_{28}I_4P_2Cd$ requires C, 23·3; H, 3·0%). *Bis-*(p-*dimethylaminophenyltrimethylphosphonium*) *cadmi-iodide* (from ethanol), m. p. 177°, molal conductance 60·0 (Found : C, 25·9; H, 3·7. $C_{22}H_{38}N_2I_4P_2Cd$ requires C, 26·1; H, 3·7%). *Bis*(*trimethylphenylarsonium*) *cadmi-iodide* (from ethanol), m. p. 193·5—194° (Found : C, 21·6; H, 2·8. $C_{18}H_{28}I_4As_2Cd$ requires C, 21·4; H, 2·8%). *Bis-*(p-*dimethylaminophenyltrimethylarsonium*) *cadmi-iodide* (from ethanol), m. p. 170·5° (Found : C, 24·0; H, 3·45. $C_{22}H_{38}N_2I_4As_2Cd$ requires C, 24·0; H, 3·45%).

Complexes of p-*Dimethylaminophenyldimethylarsine and Mercuric Iodide*.—The arsine (2·25 g., 1 mol.) in ethanol (6 c.c.) was added to a solution of mercuric iodide (4·5 g., 1 mol.) in aqueous-alcoholic potassium iodide. The resulting pale yellow precipitate was separated and extracted with ethanol. Concentration of the ethanol extract yielded colourless crystals of *bis-*(p-*dimethylaminophenyldimethylarsine*)*di-iodomercury*, m. p. 137—137·5° (Found : C, 26·6; H, 3·4. $C_{20}H_{32}N_2I_2As_2Hg$ requires C, 26·5; H, 3·5%). The yellow residue from the ethanol-extraction separated from acetone as bright yellow crystals, m. p. 148°, of the 1 : 1 complex, *di-iodobis-*(p-*dimethylaminophenyldimethylarsine*)-μμ′-*di-iododimercury* (Found : C, 17·8; H, 2·3. $C_{10}H_{16}NI_2AsHg$ requires C, 17·7; H, 2·2%).

Bis-(p-*dimethylaminophenyldimethylphosphine*)*dichlorocobalt*.—The phosphine (1·81 g., 4 mols.) in ethanol (10 c.c.) was slowly added to a well-stirred solution of cobalt(II) chloride 6-hydrate (0·6 g., 1 mol.) in ethanol (25 c.c.). During the addition the solution became dark green and no solid was formed. When the solution was boiled it became blue and a dark blue oil separated from the cooled solution. This was dissolved in hot acetone, from which it separated as a blue microcrystalline solid (m. p. 138°). The substance smelled strongly of the phosphine, even after much washing with ether and further crystallisation from acetone. After two crystallisations the *complex* melted at 140—141° (Found : C, 47·4; H, 6·3. $C_{20}H_{32}N_2Cl_2P_2Co$ requires C, 48·5; H, 6·5%). The *dibromo-complex* was prepared similarly,

and separated from acetone as deep blue needles, m. p. 153·5° (Found: C, 41·0; H, 5·5. $C_{30}H_{28}N_8Br_2P_2Co$ requires C, 41·4; H, 5·5%).

Bis(triethylphosphine)di-iodomercury.—This *compound* does not appear to have been described, and was prepared by addition of ethanolic triethylphosphine to aqueous-alcoholic potassium mercuri-iodide. It afforded colourless needles, m. p. 156—157°, from acetone (Found: C, 21·2; H, 4·8. $C_{12}H_{30}I_2P_2Hg$ requires C, 20·9; H, 4·4%).

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Calciferol and its Relatives. Part I. The Synthesis of a Model Conjugated Semicyclic Triene.

By I. T. HARRISON, B. LYTHGOE, and S. TRIPPETT.

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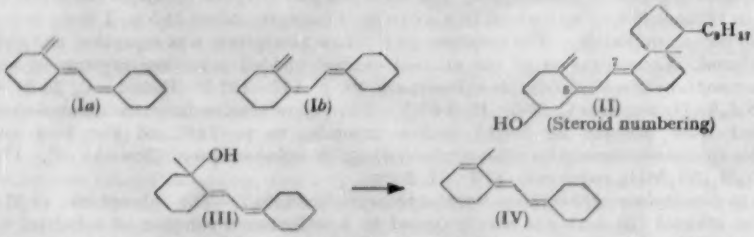
The triene, *trans*-1-2′-*cyclo*hexylidene-ethylidene-2-methylene*cyclo*hexane (I*a*), has been synthesised in two ways by application of Wittig and Schöllkopf's reaction (*Chem. Ber.*, 1954, **87**, 1318). Its unsaturated system differs from that of calciferol only in the *trans*-configuration of the central double bond.

IN all but geometric detail the structure of calciferol has been known since 1935; more recently *X*-ray studies have defined it as the *cis*-5 : *trans*-7-compound (II) (steroid numbering) (Crowfoot and Dunitz, *Nature*, 1948, **162**, 608). The simplest model substance containing the remarkable unsaturated system of the vitamin is the *cis*-triene (I*b*), but neither this nor the *trans*-isomer (I*a*) has so far been described. Earlier work aimed at the synthesis of compounds of this type (Burkhardt *et al.*, *J.*, 1938, 545, 987; 1940, 10; Dimroth, *Ber.*, 1938, **71**, 1333, 1346; Dimroth and Jonsson, *ibid.*, p. 2658; Raphael and Sondheimer, *J.*, 1950, 3185) showed that the main difficulty lay in the semicyclic character of the double bonds. A double bond semicyclic to a *cyclo*hexane ring forms a system of high energy content (for references see Brown, Brewster, and Schechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467) and in consequence ionic eliminations designed for its introduction frequently take, under Saytzeff-type control, an alternative pathway; thus dehydration of the dienol (III) gives the monoendocyclic triene (IV) instead of the desired trisemicyclic isomer (I) (Dimroth, *loc. cit.*; cf. Inhoffen, Brückner, and Gründel, *Chem. Ber.*, 1954, **87**, 1).



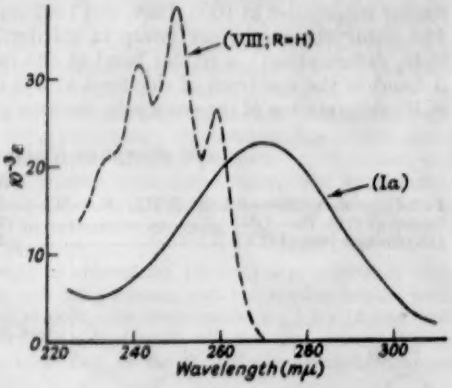
We have been engaged with experiments designed to overcome this difficulty; our first successful results were obtained by combining a proper choice of elimination method with a proper order of introduction of the three double bonds, and a synthesis of the *trans*-triene (I*a*) by this route will be described later. Wittig and Schöllkopf (*Chem. Ber.*, 1954, **87**, 1318) have meanwhile described a remarkable reaction, not subject to Saytzeff-type control, for the synthesis of olefins; it was clear to us that this reaction would be of

value in synthetic work in the calciferol field. The reaction converts a carbonyl compound into an olefin in which the carbonyl-oxygen atom is replaced by an alkylidene group by the action of an alkylidenetriphenylphosphorane :

$$R_2CO + R'CH{:}PPh_3 \longrightarrow \underset{\text{-O +PPh}_3}{R_2C{-}CHR'} \longrightarrow Ph_3PO + R_2C{:}CHR'$$

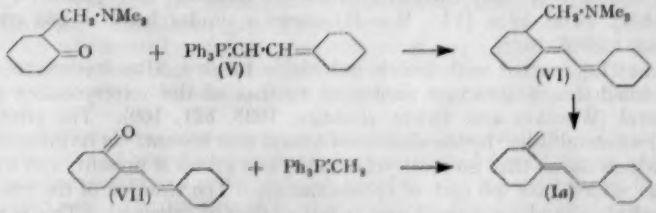
and its application to synthesis of the *trans*-triene (I*a*) by the two independent routes outlined below forms the subject of the present paper.

In suitable cases Wittig and Schöllkopf obtained mixtures of *cis*- and *trans*-olefin from their reaction; thus allylidenetriphenylphosphorane and benzaldehyde gave equal amounts of *cis*- and *trans*-1-phenylbutadiene. Since we wished if possible to obtain the *cis*-triene (I*b*) it seemed appropriate to use the reaction to set up the central double bond of the triene. For this purpose the γγ-disubstituted " allylidene " compound (V) was prepared by treatment of triphenylphosphine with 2-*cyclo*hexylidene-ethyl bromide, followed by reaction of the quaternary bromide with butyl-lithium. The quaternisation proceeded, as expected,



Light absorption of the diene (VIII; R = H) *and the triene* (I*a*) *in* EtOH.

without allylic rearrangement, since the quaternary bromide showed no infrared absorption band near 890 cm.$^{-1}$ corresponding to a methylene (:CH_2) group. It was necessary to verify that reaction of the compound (V) with ketones was not attended by allylic rearrangement; there is a similarity (by no means complete) between the behaviour of alkylidenetriphenylphosphoranes and Grignard reagents, and when a Grignard reagent



derived from a γ-substituted primary allyl halide reacts with a ketone, allylic rearrangement is known to take place (Roberts and Young, *J. Amer. Chem. Soc.*, 1945, **67**, 148; 1946, **68**, 1472). When the compound (V) reacted with *cyclo*hexanone, 1 : 2-di*cyclo*hexylidene-ethane (VIII; R = H) was obtained in good yield with no rearrangement. The structure of (VIII; R = H) was established by its absorption of 2·0 mols. of hydrogen in presence of palladium, by the formation of 1·6 mols. of *cyclo*hexanone on ozonolysis, and by its very characteristic light absorption (Figure and Table). The latter was closely similar to those

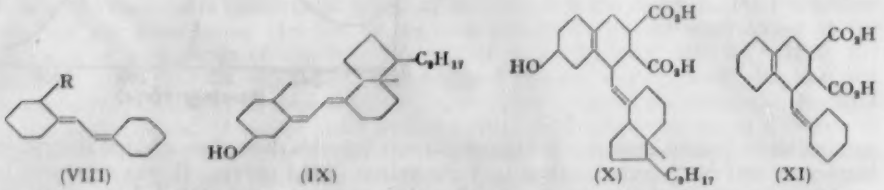
of the synthetic dienol (VIII; R = OH) (Dimroth and Jonsson, *loc. cit.*) and dihydrotachysterol (IX) (von Werder, *Z. physiol. Chem.*, **1939**, **260**, 119), both compounds being known to contain a disemicyclic conjugated diene system.

Reaction of the phosphorane (V) with 2-dimethylaminomethyl*cyclo*hexanone gave a liquid basic diene (VI) which formed a homogeneous crystalline methiodide showing light absorption similar to, though less intense than, that of the diene (VIII; R = H). Only one geometrical form (VI) had therefore been produced by the reaction; this proved later to be the *trans*-form. Wittig and Schöllkopf found that the stilbene obtained by use of their method contained much more *trans*- (70%) than *cis*-isomer (30%); this indicates that steric factors may play a part in determining the *cis* : *trans* ratio, and the absence of appreciable amounts of the *cis*-isomer of (VI) may be due to the presence of the bulky dimethylaminomethyl group.

Thermal decomposition of the quaternary hydroxide derived from (VI) gave the triene (I*a*) as a crystalline solid, which absorbed 3·1 mols. of hydrogen in the presence of palladium. Its infrared absorption spectrum (liquid film) and that of calciferol (solid film) showed important similarities. Triplet C=C stretching frequencies, such as are usually shown by conjugated trienes, occur in the spectrum of calciferol at 1610, 1634, and 1653 cm.$^{-1}$; similar frequencies at 1605, 1626, and 1647 cm.$^{-1}$ are present in that of the synthetic triene. The semicyclic methylene group in calciferol causes a band at 887 cm.$^{-1}$ (out-of-plane $=CH_2$ deformation); a similar band at 885 cm.$^{-1}$ is present in the spectrum of the triene. A band in the spectrum of calciferol at 859 cm.$^{-1}$ is almost certainly due to out-of-plane =CH– deformation of the semicyclic methine groups; in acyclic compounds this frequency

Light absorption of semicyclic conjugated dienes.

	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$
1 : 2-Di*cyclo*hexylidene-ethane (VIII; R = H)	241	31·6	250	38·1	259	26·5
Dienol (VIII; R = OH)	240	29·5	248	34·9	258	23·7
Dihydrotachysterol (IX)	242	30·2	251	40·3	261	25·9



(VIII) (IX) (X) (XI)

has the value 790—840 cm.$^{-1}$, but we have observed that this band has the higher frequency of 845—866 cm.$^{-1}$ in all the compounds so far examined which contain a semicyclic trisubstituted double bond (cf. Inhoffen, Brückner, Gründel, and Quinkert, *Chem. Ber.*, 1954, **87**, 1407). The diene (VI; R = H) shows a similar band at 863 cm.$^{-1}$ and the triene (I*a*) one at 866 cm.$^{-1}$.

The triene (I*a*) reacted with maleic anhydride to give, after hydrolysis, the dibasic acid (XI), which has a structure analogous to that of the corresponding product (X) from calciferol (Windaus and Thiele, *Annalen*, 1935, **521**, 160). The structure of the adduct (XI) was established by the absence of a band near 890 cm.$^{-1}$ in its infrared absorption spectrum, which shows that no semicyclic methylene group is present, and by the results of ozonolysis, which gave 0·6 mol. of *cyclo*hexanone. The reaction of the triene (I*a*) with maleic anhydride was about seven times as fast as that of calciferol. This is in agreement with the *trans*-configuration assigned to the triene (I*a*); the superior reactivity of *trans*-dienes in comparison with the *cis*-isomers is well known (see, *e.g.*, Crombie, *Quart. Rev.*, 1952, **6**, 126). Evidence for the *trans*-configuration of (I*a*) is also provided by its light absorption (Figure), $\lambda_{max.}$ 269·5 mμ (ε 22,700) which is more intense and at a longer wavelength than that of calciferol, which has $\lambda_{max.}$ 265 mμ (ε 18,300); this would be expected from the more fully extended nature of the chromophore of (I*a*); the lower values observed for calciferol are not due to any steric hindrance at the 7 : 8-double bond, as shown by atomic

models, but to the less fully extended chromophore and, possibly, to some slight degree of steric hindrance at the 5 : 6-double bond. The *trans*-configuration of the triene (I*a*) has further been demonstrated by its production from methylenetriphenylphosphorane and 1-2′-*cyclo*hexylidene-ethylidene*cyclo*hexanone (VII), which, from its method of preparation, almost certainly has the *trans*-configuration.

The light absorption of the synthetic triene (I*a*) provides support for the structure (II) assigned to calciferol on the basis of *X*-ray data; in particular it excludes the possibility, recently suggested by Sondheimer and Wheeler (*J. Soc. Chem. Ind.*, 1955, 714), that calciferol is the *trans*-5 : *trans*-7-isomer and that structure (II) represents precalciferol.

Modifications of the above synthetic method designed to permit the preparation of the *cis*-triene (I*b*) are being investigated.

Experimental

cyclo*Hexylidene-ethyltriphenylphosphonium Bromide.*—Triphenylphosphine (27·2 g.) was shaken with a solution of *cyclo*hexylidene-ethyl bromide (24·6 g.) in benzene at 0° until all had dissolved (10 min.). The mixture was kept at room temperature overnight, and the solid collected, washed with benzene, and dried. Recrystallisation from alcohol–benzene gave the quaternary *bromide* (30 g.), m. p. 164° (Found : Br^-, 17·5. $C_{26}H_{24}PBr$ requires Br^-, 17·8%).

*Di*cyclo*hexylidene-ethane.*—The quaternary bromide (10 g.), suspended in dry ether (100 c.c.), was treated under oxygen-free nitrogen with 1·3N-ethereal butyl-lithium (21·5 c.c.); the solid rapidly dissolved and the red solution was kept overnight at room temperature. After the addition of *cyclo*hexanone (2·56 g.) in ether (15 c.c.) the solution was shaken for 2 hr., and the ether removed by distillation and replaced by tetrahydrofuran; the solution was heated under reflux for 2 hr., and the tetrahydrofuran removed under reduced pressure. The residue was extracted with ether, and the ethereal solution washed with water, dried, and evaporated. Distillation of the residue gave *di*cyclo*hexylidene-ethane* (3 g.), b. p. 85—87°/0·1 mm., which separated from light petroleum (b. p. 40—60°) as colourless crystals, m. p. 45—47° (Found : C, 88·55; H, 11·55. $C_{14}H_{22}$ requires C, 88·3; H, 11·7%).

Ozonolysis. A solution of the diene (50 mg.) in chloroform (10 c.c.) was saturated with ozone at −25°, the chloroform removed under reduced pressure, and the residue heated with water at 95° for 10 min. The mixture was then shaken with silver oxide (2 g.) for 15 min. and filtered, and the filtrate was made alkaline with sodium hydroxide solution and extracted with ether, removal of which gave *cyclo*hexanone, identified as the 2 : 4-dinitrophenylhydrazone (113 mg.), m. p. and mixed m. p. 161°.

trans-1-*Dimethylaminomethyl*-2-2′-cyclo*hexylidene-ethylidene*cyclo*hexane.*—To a stirred suspension of *cyclo*hexylidene-ethyltriphenylphosphonium bromide (17 g.) in ether (200 c.c.) under oxygen-free nitrogen 1·3N-ethereal butyl-lithium (29 c.c.) was added, and stirring continued overnight. To the ice-cold solution 2-dimethylaminomethyl*cyclo*hexanone (5·8 g.) in ether (50 c.c.) was added, the stirred solution was allowed to warm to room temperature, and stirring was continued for 24 hr. After the addition of water (2 c.c.) an excess of dilute hydrochloric acid was added, the acid layer was separated and made alkaline with sodium carbonate, and the basic material extracted with ether. Distillation gave a fraction (1·7 g.), b. p. 105—125° (bath-temp.)/3 × 10^{-4} mm., which was treated under nitrogen with ether and methyl iodide. The *methiodide* (1·2 g.), crystallised from alcohol–benzene, had m. p. 214° (Found : N, 3·4; I, 32·3. $C_{18}H_{32}NI$, requires N, 3·6; I, 32·6%). Light absorption in alcohol : $\lambda_{max.}$ 242, 250, and 259 mμ ($10^{-3}\varepsilon$ 27·8, 31·0, and 20·3).

trans-1-2′-cyclo*Hexylidene-ethylidene*-2-*methylene*cyclo*hexane.*—(*a*) The above methiodide (1·2 g.) in water (30 c.c.) was shaken with silver oxide (from 3·6 g. of silver nitrate) for 4 hr., the filtered solution evaporated under reduced pressure, and the residue distilled at 60—95° (bath-temp.)/10^{-4} mm. The distillate (250 mg.) crystallised from light petroleum (b. p. 40—60°) at −40°, giving the *triene* as colourless prisms (165 mg.), m. p. 14—16° (Found : C, 89·3; H, 10·7. $C_{15}H_{22}$ requires C, 89·0; H, 11·0%).

A repetition of this experiment with crude methiodide obtained from the mother liquors gave as product a mixture containing a small amount of the above triene and larger amounts of other unsaturated materials which showed rapidly rising absorption in the far ultraviolet region; no isomer absorbing near 265 mμ was detectable.

(*b*) To a suspension of methyltriphenylphosphonium bromide (1·9 g.) in ether (50 c.c.) under oxygen-free nitrogen 1·3N-ethereal butyl-lithium (4·1 c.c.) was added and the mixture

stirred for 4 hr. A solution of 2-2′-*cyclo*hexylidene-ethylidene*cyclo*hexanone (1·0 g.) in ether (10 c.c.) was then added and the mixture stirred overnight, filtered, washed with water, dried, and evaporated. Distillation at 90° (bath-temp.)/5×10^{-5} mm. gave the triene (0·55 g.) which after crystallisation from light petroleum (b. p. 40—60°) had m. p. 14—16° and showed ultraviolet and infrared absorption identical with that prepared by method (*a*). A portion of the triene (0·1 g.) was isomerised by aqueous-alcoholic 0·25% sulphuric acid at room temperature for 22 hr., giving an isomeric triene, $\lambda_{max.}$ (alcohol) 284 mμ (ε 39,400).

Reaction of the trans-*Triene with Maleic Anhydride.*—(*a*) A mixture of the triene (162 mg.), maleic anhydride (95 mg.), and benzene (10 c.c.) was heated under reflux for 3½ hr., filtered, and evaporated, and the residue heated at 100° for 40 min. with 10% aqueous sodium hydroxide (15 c.c.). The cooled and acidified solution was extracted with ether, removal of which gave 1-cyclo*hexylidenemethyl*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*octahydronaphthalene*-2 : 3-*dicarboxylic acid* (XI) (150 mg.) which, crystallised from alcohol, had m. p. 178—180° (decomp.) (Found : C, 72·1; H, 8·0. $C_{19}H_{28}O_4$ requires C, 71·7; H, 8·2%).

Ozonolysis of a sample (76·7 mg.) in chloroform (10 c.c.) in the usual manner gave *cyclo*hexanone as the sole neutral product, isolated as the 2 : 4-dinitrophenylhydrazone (34 mg.).

(*b*) For comparison of the rates of reaction of the triene and calciferol with maleic anhydride, two solutions were prepared containing maleic anhydride ($5{\cdot}2 \times 10^{-3}$ mole/l.); to one was added calciferol ($3{\cdot}69 \times 10^{-5}$ mole/l.), to the other the triene ($4{\cdot}62 \times 10^{-5}$ mole/l.). Both solutions were kept at 18°, and the logarithms of their respective optical densities at 265 and 269 mμ measured and plotted against time. Two straight lines were obtained, the ratio of whose gradients (6·9) gave the ratio of the velocity constants of the two reactions.

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NOTES.

*The Kinetics of Alkyl–Oxygen Fission in Ester Hydrolysis. Part IV.** tert.-*Butyl Formate in Aqueous Acetone.*

By V. R. Stimson.

[Reprint Order No. 6393.]

The rate of the acid-catalysed hydrolysis of *tert.*-butyl formate is proportional to the concentrations of both ester and acid catalyst. A plot of rate against acid concentration shows that no uncatalysed reaction of comparable rate occurs. A small rise in k_1 (*ca.* 5% from 30 to 70% reaction) found during the reaction is attributed to autocatalysis by the formic acid produced. The value of $\log_{10}10^6k_1/C_A$ (sec.$^{-1}$) is 5·47 at 100° in 60% acetone. This represents a rate 22 times that of *tert.*-butyl benzoate and 2 : 4 : 6-trimethylbenzoate and comparable with that of ethyl and methyl formate; k_1/C_A for these two esters is $2{\cdot}2 \times 10^{-1}$ and $2{\cdot}0 \times 10^{-1}$ sec.$^{-1}$, respectively (calc. from the results at 25° of Newling and Hinshelwood, *J.*, 1936, 1357), and for *tert.*-butyl formate $3{\cdot}0 \times 10^{-1}$ sec.$^{-1}$ (calc.).

The Arrhenius equation is accurately followed, the activation energy being 16·3 ± 0·5 kcal./mole and $\log_{10}A$ (sec.$^{-1}$) 9·04. The value of E is quite different from that found for *tert.*-butyl benzoate and 2 : 4 : 6-trimethylbenzoate (*ca.* 30 kcal./mole; Parts I, *J.*, 1954, 2848; II, *J.*, 1955, 2010; and III *), for which mechanism $A_{AL}1$ has been suggested, but is almost identical with that found for methyl and ethyl formate (15·6 kcal./mole; Newling and Hinshelwood, *loc. cit.*), and lies within the range of values (15—17 kcal./mole, cf. Part I) generally found for hydrolysis of methyl and ethyl esters of aliphatic acids which are hydrolysed by mechanism $A_{AC}2$. Hence it is suggested that

* Part III, *J.*, 1955, 2673.

the acid hydrolysis of *tert.*-butyl formate occurs largely if not wholly by mechanism $A_{AC}2$ and that a transition in mechanism from $A_{AL}1$ to $A_{AC}2$ occurs in the series 2 : 4 : 6-trimethylbenzoate, benzoate, acetate, and formate, between the benzoate and formate for the *tert.*-butyl ester.

The result is that expected from an analysis (as in Part III) of rates of hydrolysis of formates by $A_{AC}2$ and *tert.*-butyl esters by $A_{AL}1$, and agrees with the observation that diphenylmethyl formate undergoes acyl–oxygen fission (Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686) even though diphenylmethyl shows strong electron-releasing properties in S_N reactions.

First-order rate constants (k_1) for hydrolysis of tert.*-butyl formate in* 60% *acetone.*

(C_A and C_E are the concentrations of hydrochloric acid and ester respectively.)

Temp.	10^2C_A (mole/l.)	10^2C_E (mole/l.)	10^3k_1 (min.$^{-1}$)	k_1/C_A (min.$^{-1}$ l. mole^{-1})	Temp.	10^2C_A (mole/l.)	10^2C_E (mole/l.)	10^3k_1 (min.$^{-1}$)	k_1/C_A (min.$^{-1}$ l. mole^{-1})
97·1°	0·30	1·53	45	15·0	84·4	0·17	1·90	11·3	6·6
,,	0·28	1·93	41	14·6	80·3	0·79	1·73	41	5·2
,,	0·28	2·00	42	14·8	73·4	0·82	1·56	28·0	3·4
,,	0·15	1·67	22·4	14·5	72·3	0·17	1·62	4·9	2·9
,,	0·13	1·43	19·7	15·3					

Experimental.—Preparation of tert.*-butyl formate.* (a) Samples prepared by Bateman and Hughes's method (*J.*, 1940, 935) contained small amounts (up to 10%) of free acid. (b) A mixture of dried, fractionated *tert.*-butyl alcohol (m. p. 24·5—25·0°; 25 ml.) and formic acid ("AnalaR," anhyd.; 25 ml.) after standing overnight was quickly distilled, 15 ml. of b. p. <90° being collected, which on fractionation through an 8-in. column packed with Fenske helices gave 3 g. of product having b. p. 76°/680 mm. and containing 85% of ester (calc. from the acid produced on complete hydrolysis) and <1% of free acid, which values were unchanged on redistillation. Hydrolysis produced a reducing substance (0·88 mol. as formic acid by permanganate titration; Vogel, "Quantitative Inorganic Analysis," Longmans, Green and Co., 1944, p. 361). *tert.*-Butyl alcohol did not interfere with the estimation. The analysis (Found: C, 58·3; H, 11·0. Calc. for $C_5H_{10}O_2$: C, 58·7; H, 9·9%) is of the right order.

Several samples were made in this way and had purities of 85—90% and gave consistent rate constants. Possible impurities are *tert.*-butyl alcohol, water, and traces of di*iso*butene which would not be expected to interfere with the kinetics.

The experimental procedure was that described in Parts I and II except that *a* was found from the titre on complete hydrolysis.

The microanalysis was carried out by Dr. W. Zimmermann, of C.S.I.R.O., Melbourne.

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Tetracarbonyliron Bisphenylacetylide.

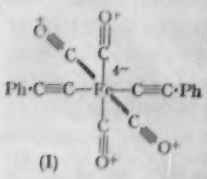
By E. R. H. JONES, P. C. WAILES, and M. C. WHITING.

[Reprint Order No. 6457.]

PRELIMINARY information on war-time German work implied that while iron carbonyl by itself was inert to acetylene under acidic conditions, it did react to some extent when nickel carbonyl was present (see Copenhaver and Bigelow, "Acetylene and Carbon Monoxide Chemistry," Reinhold, New York, 1949, pp. 251, 292, 293). Recently Reppe and his colleagues have described much work on metal carbonyl–acetylene reactions, and although the use of acrylic ester as catalyst is said to induce a reaction between acetylene and iron carbonyl, more acrylate being formed, no mention is made of the use of mixed carbonyls (Reppe, *Annalen*, 1953, **582**, 30).

Attempts to effect reaction between iron carbonyl and phenylacetylene under the conditions (aqueous-ethanolic acetic acid at 60—80°) found optimal for nickel carbonyl

(Jones, Shen, and Whiting, *J.*, 1950, 230) proved unsuccessful. Nickel carbonyl was then added to the mixture, an exothermal reaction occurred, and atropic acid was formed; the yield, however, never exceeded that expected from the nickel carbonyl alone, the stoicheiometry postulated by Jones, Shen, and Whiting (*J.*, 1951, **766**) being assumed to hold. A sparingly soluble, neutral product separated from the mixture in small yield, giving analytical data appropriate for $C_{20}H_{10}O_4Fe$ or $C_{20}H_{12}O_4Fe$. The latter hardly permits rationalisation, but the former suggests structure (I), which is isoelectronic with $Cr(CO)_6$, $Fe(C{\equiv}NMe)_4(CN)_2$, and $Fe(CN)_6^{4-}$, possessing a complete 36-electron shell about the central atom, a feature almost invariably associated with great stability in complexes of the transition metals. This substance was in fact extremely stable; it showed no sign of decomposition at 220°, and it was recovered unchanged after several hours in boiling 20% sulphuric acid. It was, however, readily decomposed by irradiation of its solutions, with the precipitation of ferric oxide; in this it closely resembles ferrocene, which is also otherwise extremely stable. It reacted with alkali, giving a red solution from which some of the original complex could be recovered on acidification. Chromium hexacarbonyl also reacts with alkalis (Rhomberg and Owen, *J. Amer. Chem. Soc.*, 1951, **73**, 5904), giving a hydrocarbonyl $Cr(CO)_5H_2$ which readily disproportionates to the hexacarbonyl.



(I)

Several attempts at more rational syntheses of (I), including treatment of iron pentacarbonyl with phenylmagnesium bromide, or of the potassium salt of iron carbonyl hydride with iodophenylacetylene, failed to give recognisable products. There appears to be no close analogy between the complex described above and any of the numerous acetylene-carbonyl complexes reported by Reppe and Vetter (*Annalen*, 1953, **582**, 133).

Experimental.—Phenylacetylene (7·1 g.), ethanol (20 c.c.), water (1·0 c.c.), and glacial acetic acid (4·2 c.c.) were heated to 65° while a mixture of nickel carbonyl (1·4 g., 1·0 c.c.) and iron pentacarbonyl (5·5 g., 3·8 c.c.), contained under a layer of ethanol in a dropping funnel, was added slowly with stirring. After a short induction period an exothermal reaction began, and the temperature remained at 60—65° without external heating. Heating was then resumed and continued for 2 hr. On cooling of the mixture, the *complex* separated and after addition of dilute sulphuric acid and ether was collected by filtration; crystallisation from benzene or dilute acetic acid gave fine yellow needles, (0·35 g.) m. p. 222—222·5° (Found: C, 64·5, 64·4; H, 3·1, 3·0; Fe, 15·5. $C_{20}H_{10}O_4Fe$ requires C, 64·85; H, 2·7; Fe, 15·1. $C_{20}H_{12}O_4Fe$ requires C, 64·5; H, 3·25; Fe, 15·0%). (Iron was determined on 130 mg. of material, after dissolution in nitric acid, heating for several hours, precipitation as ferric hydroxide, and weighing as the oxide).

In ethanol the complex showed a broad absorption maximum at 3300 Å (ε = 6500) and rising absorption with inflexions at *ca.* 2320, 2480, 2900, and 2960 Å (ε = 22,000, 19,000, 9,000, and 8000, respectively); absorption was still appreciable at 4000 Å. In the infrared (Nujol suspension), bands attributable to phenyl groups were observed at 3070, 3030, 1615, 770, 746, and 688 cm^{-1} and to ·C≡C· and ·C≡O (metal carbonyl type) stretching modes at 2070, 2010, and 1992 $cm.^{-1}$. Absorption at *ca.* 3300 $cm.^{-1}$ (acetylenic CH stretching) was absent.

One of us (P. C. W.) thanks the Commonwealth of Australia Scientific and Industrial Research Organisation for a Maintenance Grant.

THE UNIVERSITY, MANCHESTER. [*Received, May 24th*, 1955.]

Organosilicon Compounds. Part XVI. The Alkaline Hydrolysis of Triorganomonosilanes.*

By J. E. Baines and C. Eaborn.

[Reprint Order No. 6474.]

The theoretical significance of the kinetics of the alkaline hydrolysis of organosilicon hydrides (Price, *J. Amer. Chem. Soc.*, 1947, **69**, 2600; Gilman and Dunn, *ibid.*, 1951, **73**, 3404; Gilman, Dunn, and Hammond, *ibid.*, p. 4499; Kaplan and Wilzbach, *ibid.*, 1952, **74**, 6152; 1955, **77**, 1297) and the value of the reaction for indicating the steric effects of substituents on ease of nucleophilic substitution at silicon (*e.g.*, West, *ibid.*, 1954, **76**, 6015) prompt us to record some fragmentary observations on the reactions of triorganomonosilanes with aqueous-alcoholic alkalis.

Salt Effects.—Although Price (*loc. cit.*) states that the specific rate constant, k_s ($= k_1/[OH^-]$, where k_1 is the observed first-order rate constant), for alkaline solvolysis in aqueous alcohol is independent of the concentration of alkali it appears from his results that there is a considerable salt effect. For the solvolysis of triethylsilane (*ca.* 0·07M) in 94·5 vol.-% ethanol–water (s.g. 0·8180 at 60° F) at 34·9° we have examined the effect of varying the sodium hydroxide concentration and of adding sodium iodide or perchlorate. Good first-order kinetics during a run are observed for the whole range of salt concentration, but Table 1 shows that k_s falls markedly as the salt concentration is raised. At a given

Table 1.

[NaOH] (M)	0·0497	0·0740	0·100	0·201	0·100	0·302	0·201
Added salt	—	—	—	—	NaI	—	NaI
[Added salt] (M)	—	—	—	—	0·102	—	0·102
[Total salt] (M)	0·0497	0·0740	0·100	0·201	0·202	0·302	0·303
k_s (min.$^{-1}$ mole^{-1} l.)	0·124	0·117	0·110	0·094	0·092	0·081	0·082
[NaOH] (M)	0·201	0·403	0·201	0·804	0·201	1·126	
Added salt	$NaClO_4$	—	NaI	—	NaI	—	
[Added salt] (M)	0·098	—	0·203	—	0·600	—	
[Total salt] (M)	0·299	0·403	0·404	0·804	0·801	1·126	
k_s (min.$^{-1}$ mole^{-1} l.)	0·082	0·076	0·075	0·054	0·51	0·043	

salt concentration, k_s is independent of which sodium salts are present, and thus disturbance of the equilibrium, $HO^- + EtOH \rightleftharpoons EtO^- + H_2O$, by added hydroxide ion is not a major factor.

The straight line, $\log k_s = -0·79 - 0·55\,\mu^{\frac{1}{2}}$ (μ = ionic strength), fits the data excellently.

The solvolysis of triethylsilane is faster with potassium hydroxide than with sodium hydroxide in the range studied ([KOH] = 0·2—1·1M), increasingly so as the alkali concentration is raised; at an alkali concentration of 1·125M the reaction is 1·35 times as fast with potassium hydroxide as with sodium hydroxide. The line, $\log k_s = -0·87 - 0·34\,\mu^{\frac{1}{2}}$, fits the data shown in Table 2.

Table 2.

[KOH] (M)	0·200	0·280	0·375	0·563	0·750	1·126
k_s (min.$^{-1}$ mole^{-1} l.)	0·096	0·90	0·82	0·071	0·068	0·058

Clearly the salt effects must be considered when rates of alkaline hydrolysis are used to compare reactivities of various organosilicon hydrides. The magnitude of the salt effect, the dependence of $\log k$ on $\mu^{\frac{1}{2}}$ and not on μ, and the higher rates with potassium than with sodium hydroxide (which suggest that activities should be used in place of concentrations) fit a hypothetical reaction between a negative ion and an entity having a partial fractional positive charge rather than a reaction between an ion and a neutral molecule. The nature

* Part XV, *J.*, 1955, 3306.

of the transition state is fairly well understood (Kaplan and Wilzbach, *loc. cit.*) but seems to offer no explanation of our results.

Formation of the Silanol Anion.—Aryldimethylsilanes are more reactive than trialkylsilanes in alkaline hydrolysis, and for rate studies lower concentrations of alkali have to be used, so that the organosilane is present in large excess. Under these conditions the first-order plot based on the evolved hydrogen shows a continuous curvature in the direction of falling rate. That this is due to formation of the aryldimethylsilanol (which removes hydroxide or ethoxide ion by formation of the silanol anion, *e.g.*, $Me_2ArSiOH + OH^- \rightleftharpoons Me_2ArSiO^- + H_2O$) was shown by adding the appropriate silanol; this caused a marked fall in the initial rate and led to a first-order plot closer to a straight line. The magnitude of the effect is shown in Table 3, approximate initial first-order rate constants being listed.

TABLE 3.

Ar	Ph		*p*-Me·C_6H_4	
[KOH] (M)	0·0153	0·0153	0·0186	0·0186
[$ArMe_2SiH$] (M)	0·051	0·051	0·082	0·061
[$ArMe_2SiOH$] (M)	—	0·058	—	0·056
k_1 (min.$^{-1}$)	0·097	0·043	0·063	0·040

The first-order plots are curved even for trialkylsilanes when these are present initially in few-fold excess over the alkali (*e.g.*, in the reaction of 0·24M-triethylsilane with 0·07M-sodium hydroxide).

Reactivities of Triorganosilanes.—The rates of solvolysis of several trialkylsilanes in 94·5 vol.-% ethanol–water containing 1·120M-sodium hydroxide are shown in Table 4, along with the constants of the Arrhenius equation, $k_1 = A \exp(-E/RT)$.

TABLE 4.

R	Et	Pr^n	Bu^n	Bu^i	Pr^i
k_1 (min.$^{-1}$) at 34·9°	0·0633	0·0253	0·0174	0·00261	0·00139
k_1 (min.$^{-1}$) at 23·3°	0·226	0·00855	0·00587	0·00852	0·00431
E (kcal./mole)	15·9	16·8	16·8	17·3	18·1
log A *	10·1	10·3	10·2	9·7	10·0
Relative rates (34·9°)	100	40	27	4·1	2·2

* Calc. for time in min.

The order of decreasing reactivity of the trialkylsilanes is that of increasing electron release in the radical R, which is known to lead to a fall in rate (see below), but probably steric hindrance is mainly responsible for the sequence observed. It is surprising that the reactivities of tri*iso*butyl- and tri*iso*propyl-silane are so close since distinctly greater steric hindrance would be expected for nucleophilic attack on the latter compound.

While accurate comparison is impossible, dimethylphenylsilane appears to be roughly 50 times as reactive as triethylsilane, and thus (using Price's figures, *loc. cit.*) about 14 times as reactive as dimethyl-*n*-propylsilane. Dimethyl-*p*-tolyl- is less reactive than dimethylphenyl-silane, so that electron supply towards silicon slows the solvolysis, as found for triarylsilanes in moist piperidine (Gilman and Dunn, *loc. cit.*).

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UNIVERSITY COLLEGE, LEICESTER. [*Received, June 1st,* 1955.]

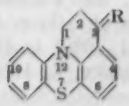
Reactions with Girard Reagents.

By Alexander Mackie and Anand L. Misra.

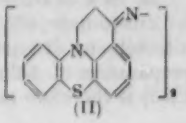
[Reprint Order No. 6495.]

Mackie and Misra (*J.*, 1955, 1281) reported that reaction of 2 : 3-dihydro-3-oxo-1*H*-pyrido-[3 : 2 : 1-*kl*]phenothiazine (I*a*) with Girard reagent " P " (carbohydrazidomethylpyridinium chloride) in presence of absolute ethanol–acetic acid gave two products. One was the expected pyridinium acetylhydrazono-derivative (I*b*), soluble in water, methanol, and ethanol, insoluble in acetone and non-hydroxylic solvents, and hydrolysed by N-hydrochloric acid to the original ketone (I*a*). The other product (A), was obtained as orange-yellow plates, m. p. 299—300° (decomp.); it was insoluble in water, methanol, ethanol, and acetone, sparingly soluble in chloroform and benzene, very soluble in dioxan, chlorobenzene, and pyridine, and contained no halogen. Although unchanged by boiling concentrated hydrochloric acid or concentrated aqueous potassium hydroxide, it was hydrolysed to the ketone (I*a*) by refluxing in dioxan with concentrated hydrochloric acid.

It is suggested that the compound has the structure (II) (Found : C, 71·2; H, 4·3; S, 12·2. $C_{30}H_{22}N_4S_2$ requires C, 71·7; H, 4·4; S, 12·7%), and is probably formed by partial hydrolysis



(I*a*), R = :O
(I*b*), R = :N·NH·CO·CH_2·N$^+$$C_5H_5$}Cl$^-$
(I*c*), R = :N·NH·CO·CH_2·N$^+$$Me_3$}Cl$^-$
(I*d*), R = :N·NH·COMe



(II)

of some of (I*b*) in ethanol–acetic acid to give the substituted hydrazine, which in turn reacts with unchanged ketone (I*a*) to give compound (A). This was substantiated by causing equimolecular quantities of (I*a*) to react with (I*b*) under similar conditions, whereupon crystals separated from the reaction mixture in small yield, obtained as orange-yellow plates from chlorobenzene, m. p. 295—297° (decomp.) (Found : C, 71·5; H, 4·5%). The structure was further confirmed by the formation of the same product, m. p. 295—297° (decomp.) (Found : C, 70·9; H, 4·3%), by condensation of the ketone (I*a*) in absolute ethanol–acetic acid with hydrazine sulphate in presence of sodium acetate. The reaction of (I*a*) with acetohydrazide (Curtius and Hofman, *J. prakt. Chem.*, 1896, **53**, 524) under the same conditions as the reaction of (I*a*) with Girard reagent " P " afforded only the 3-*acetohydrazono*-2 : 3-*dihydro-derivative* (I*d*), yellow needles from chlorobenzene, m. p. 258—259° (Found : C, 65·8; H, 4·5. $C_{17}H_{15}ON_3S$ requires C, 66·0; H, 4·9%), which was hydrolysed to the ketone (I*a*) with warm concentrated hydrochloric acid.

Condensation of the ketone (I*a*) with Girard reagent " T " (carbohydrazidomethyltrimethylammonium chloride) under the same conditions as with reagent " P " gave two compounds, (i) the normal product (I*c*), yellow stellate needles (turned orange on keeping) from absolute ethanol, m. p. 200° (decomp.) (m. p. lowered on keeping) (Found : C, 55·1; H, 6·0. $C_{20}H_{23}ON_4ClS,2H_2O$ requires C, 54·7; H, 6·1%); (ii) the compound (A), orange-yellow plates from chlorobenzene, m. p. 295—297° (decomp.) (Found : C, 71·1; H, 4·3%).

The infrared spectra of compounds (I*b*) and (A) were determined, but owing to the complexity of these molecules, interpretation of the spectra proved difficult. However, one absorption band, with sharp peak, at 1580 cm.$^{-1}$, in the spectrum of compound (A), but absent from that of compound (I*b*), was very conspicuous. This corresponds to C=C stretching vibrations, and it is known that a direct linkage of an unsaturated group to the nucleus enhances the intensity of this band to such a degree that it becomes more pronounced in the spectrum, thus enabling the detection of conjugation with the rings. Compound (I*b*) has NH (3450 cm.$^{-1}$) and CO·NH (1668 cm.$^{-1}$) absorption bands, both absent in the spectrum of compound (A). The proposed structure of compound (A) is in agreement with these observations.

We thank the Council of Scientific and Industrial Research (India) for the award (to A. L. M.) of an Assam Oil Co. Scholarship, Professor F. Bell for helpful criticism, and Dr. L. J. Bellamy, Ministry of Supply, Chemical Inspectorate, for the infrared determinations.

Heriot-Watt College, Edinburgh. [*Received, June 10th*, 1955.]

The Nitration of o-*Fluorotoluene.*

By H. Suschitzky.

[Reprint Order No. 6509.]

Schiemann (*Ber.*, 1929, **62**, 1794) and Varma *et al.* (*J. Indian Chem. Soc.*, 1944, **21**, 112) reported that, by nitration of *o*-fluorotoluene with fuming nitric acid, they obtained a mixture of 2-fluoro-5-nitro- (72%) and 2-fluoro-6-nitro-toluene (14%), which they separated by fractional distillation.

This reaction was re-investigated, because the nitro-isomers are useful intermediates for the synthesis of certain heterocyclic structures. The oily nitration product was treated with piperidine or with *cyclo*hexylamine to facilitate separation and identification of the products. The nature of the piperidino- and *cyclo*hexylamino-compounds suggested the presence of only 2-fluoro-5-nitrotoluene (84%). However, a portion of the nitration product was unaffected by this treatment and yielded, on reduction and benzoylation, 4-benzamido- and 6-benzamido-2-fluorotoluene, the structure of the latter being shown by cyclisation of its nitroso-derivative to a fluoroindazole.

In view of these results (2-fluoro-5-nitro-, 84%; 2-fluoro-4-nitro-, 10%; and 2-fluoro-6-nitro-toluene, 6%), Schiemann's 2-fluoro-6-nitrotoluene must be a mixture of 2-fluoro-6-nitrotoluene (1 part) and 2-fluoro-4-nitrotoluene (*ca.* 2 parts). The yield (20%) in the preparation of 4-fluoroindole-2-carboxylic acid (Allen, Brunton, and Suschitzky, *J.*, 1955, 1283) is therefore raised to 34%.

Experimental.—*5-Nitro-2-piperidinotoluene.* The oily mixture of nitro-compounds (29 g.) obtained by nitration of *o*-fluorotoluene (Schiemann, *loc. cit.*) was heated on a water-bath with piperidine (50 c.c.) for 10 hr. and the reaction mixture was then added to concentrated hydrochloric acid (200 c.c.) cooled by a freezing mixture. An oily layer separated which was repeatedly extracted with chloroform. The acidic layer on dilution with water afforded yellow needles of *5-nitro-2-piperidinotoluene*, m. p. 48° (from benzene) (33·5 g., corresponding to 84% of 2-fluoro-5-nitrotoluene) (Found: C, 65·5; H, 7·3; N, 12·4. $C_{12}H_{16}O_2N_2$ requires C, 65·5; H, 7·3; N, 12·7%).

2-cyclo*Hexylamino-5-nitrotoluene.* Warming of the nitration product (34 g.) with *cyclo*hexylamine (65 g.) on a water-bath (12 hr.) followed by treatment with concentrated hydrochloric acid (180 c.c.) and removal of an oily layer as described above, yielded 2-cyclo*hexylamino-5-nitrotoluene* as yellow needles, m. p. 93° (ethanol) (44·4 g., corresponding to 82% of 2-fluoro-5-nitrotoluene) (Found: C, 66·4; H, 7·6; N, 11·9. $C_{13}H_{18}O_2N_2$ requires C, 66·6; H, 7·7; N, 11·9%).

6-*Benzamido-2-fluorotoluene.* A portion of the oil (5 g.) obtained from both the above preparations was reduced with stannous chloride (30 g.) dissolved in a mixture of concentrated hydrochloric acid (85 g.) and ethanol (20 c.c.). Benzoylation of the purified reduction product (7·1 g.) (steam distillation) gave a white solid which was fractionately crystallised from a minimum of boiling ethanol. The insoluble portion could be cyclised to a fluoro-indazole (see below) and was, therefore, 6-*benzamido-2-fluorotoluene* (2·6 g.), m. p. 158—159° (needles from ethanol) (Found: C, 73·8; H, 5·3; N, 6·3. $C_{14}H_{12}ONF$ requires C, 73·8; H, 5·1; N, 6·0%).

4-*Benzamido-2-fluorotoluene.* From the mother-liquors of the above fractionation 4-*benzamido-2-fluorotoluene* separated as white plates (4·3 g.), m. p. 124—128° (m. p. 127—128° after chromatography from benzene on alumina). The product did not depress the m. p. of a sample prepared from authentic 4-amino-2-fluorotoluene (Schmelkes and Rubin, *J., Amer. Chem. Soc.*, 1944, **66**, 1631) (Found: C, 73·6; H, 5·0; N, 5·9. $C_{14}H_{12}ONF$ requires C, 73·8; H, 5·1; N, 6·0%).

4-*Fluoroindazole.* 6-Benzamido-2-fluorotoluene (2 g.) was nitrosated (4·5 hr.) in a mixture of glacial acetic acid (12 c.c.) and acetic anhydride (10 c.c.). When the product, obtained by pouring the reaction mixture on to crushed ice, was crystallised from cold acetic anhydride the N-*nitroso-compound* (2 g.) separated, m. p. 65° (decomp.) (Found: N, 11·2. $C_{14}H_{11}O_2N_2F$ requires N, 10·7%). A solution of this compound (2 g.) in benzene (20 c.c.; sodium-dried) was kept at room temperature for two days; the solid, obtained by extracting the benzene

layer with concentrated hydrochloric acid followed by basification with ammonia solution, was steam-distilled and yielded 4-*fluoroindazole* as white needles, m. p. 130—131° (ethanol) (Found : C, 61·7; H, 3·3; N, 20·3. $C_7H_5N_2F$ requires C, 61·8; H, 3·7; N, 20·6%).

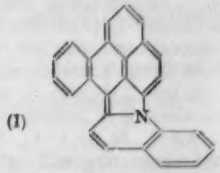
ROYAL TECHNICAL COLLEGE, SALFORD, LANCS. [*Received, June 15th*, 1955.

Decomposition of Quinaldic and meso*Benzanthrone-3-carboxylic Acids in the Presence of* meso*Benzanthrone.*

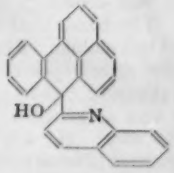
By WILLIAM BRADLEY and HARRY E. NURSTEN.

[Reprint Order No. 6522.]

THE thermal decomposition of quinaldic acid affords the 2-quinolyl anion and this reacts with quinoline to form 2 : 2′-diquinolyl (Brown and Hammick, *J.*, 1949, 173). It was of interest to investigate the same decomposition in the presence of *meso*benzanthrone which is known to undergo substitution by anions *ortho* and *para* to the carbonyl group (Bradley, *J.*, 1948, 1175). The reaction did not take the expected course but there resulted a crystalline product, $C_{26}H_{15}N$, which appeared to be a pyrrocoline derivative (I). It is possible that the first product of the reaction is 2-(7-hydroxy-7-benzanthryl)quinoline (II) which then undergoes cyclisation with loss of water. The expected products, 4- or 6-2′-quinolyl*meso*benzanthrone, were not encountered.

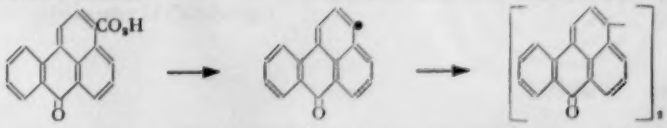


(I)



(II)

*meso*Benzanthrone-3-carboxylic acid is readily decarboxylated when heated in quinoline with copper powder (Backhouse and Bradley, *J.*, 1955, 849), but the kinetics of the reaction have not been investigated. When the acid is decomposed in the presence of *meso*benzanthrone, di-3-*meso*benzanthronyl is formed. This product might result by (*a*) the formation of 3-*meso*benzanthronyl radicals which then unite or (*b*) the formation of 3-*meso*benzanthronyl anions which then attack free *meso*benzanthrone. Direct substitution by anions at the 3-position of *meso*benzanthrone, though possible in theory, has not been previously observed in practice, and for this reason a radical mechanism appears to be the more probable.



Experimental.—Quinaldic acid and meso*benzanthrone.* A mixture of quinaldic acid (5 g.) and *meso*benzanthrone (25 g.) was heated for 2 hr. at 180°. The product was dissolved in hot benzene (400 c.c.); a residue (0·055 g.) remained. On being cooled the brown solution gave *meso*benzanthrone (17 g.), and an additional amount (7·3 g.) of less pure material (*A*) separated when the mother-liquor was concentrated to 50 c.c. The mother liquor from the concentrated solution was then extracted with hydrochloric acid. After being made alkaline and steam-distilled the acid solution afforded quinoline (2·2 c.c.) and non-volatile, brown needles (0·05 g.) of 2 : 2′-diquinolyl, m. p. 183—190° (m. p.s below 300° are corrected) (picrate, m. p. 213—213·5°). Brown and Hammick record m. p. 192·5—193·5° and m. p. 211—212° for the base and picrate, respectively. The residue (0·6 g.) which remained on evaporation of the acid-washed

benzene solution was chromatographed from benzene on alumina. Two bands resulted, a brown band due to *meso*benzanthrone and a more mobile, yellow band. Elution of the latter with benzene afforded a solid (0·15 g.) which crystallised from ethanol in yellow needles, m. p. 228—229° [Found : C, 90·5, 90·3; H, 4·4, 4·5; N, 4·0, 4·05%; *M* (Rast), 346 ± 30. $C_{24}H_{15}N$ requires C, 91·5; H, 4·4; N, 4·1%; *M*, 341]. More (0·41 g.) of the same *product* was obtained by similar purification of (*A*). It gave a yellow solution (yellow-green fluorescence) in pyridine, unchanged on the further addition of methanolic potassium hydroxide, alone or with sodium dithionite. It was unaffected when heated with potassium hydroxide for 10 min. at 250°. It did not react with methyl iodide, methyl toluene-*p*-sulphonate, or acetic anhydride in benzene. It was insoluble in hydrochloric acid, but dissolved in concentrated sulphuric acid to give a reddish-violet solution which became bluer when heated or kept. Light absorption of a 0·002% solution in alcohol (10^{-4} ε values in parentheses) : $\lambda_{max.}$ 211 (4·04), 215 (4·17), 218 (3·43), 220 (3·60), 253 (3·43), 271 (1·88), 290 (3·12), 292 (3·14), 334 (0·88), 351 (0·89), 368 (0·87), 420 (1·95), 440 (2·49), and 468 mμ (1·57); $\lambda_{min.}$ 212 (3·96) 216 (3·35), 219 (3·38), 236 (2·04), 270 (1·87), 275 (1·80), 291 (3·10), 327 (0·84), 342 (0·75), 360 (0·60), 380 (0·59), 429 (1·74), and 456 mμ (1·12).

meso*Benzanthrone-3-carboxylic acid and* meso*benzanthrone.* Ethyl *meso*benzanthrone-3-carboxylate [5 g.; m. p. 154° (Found : C, 80·0; H, 4·65. Calc. for $C_{20}H_{14}O_3$: C, 79·5; H, 4·6%); Backhouse and Bradley, *loc. cit.*] was refluxed for 3 hr. with 5% aqueous sodium hydroxide (50 c.c.) and alcohol (5 c.c.). Acidification of the resulting solution and crystallisation of the precipitate from nitrobenzene afforded *meso*benzanthrone-3-carboxylic acid (4·5 g.; m. p. 347—348°) (Found : C, 78·4; H, 3·6. Calc. for $C_{18}H_{10}O_3$: C, 78·8; H, 3·6%).

*meso*Benzanthrone-3-carboxylic acid (3 g.) and *meso*benzanthrone (15 g.; purified by chromatography on alumina) were heated for 5 hr. at 290—320°. The cooled product was extracted with hot chlorobenzene (300 c.c.), and the extract filtered from a residue (0·18 g.). On being cooled the solution afforded *meso*benzanthrone (11·22 g.), and more (4·62 g.) separated when the mother-liquor was concentrated to 50 c.c. The remaining solution was chromatographed on alumina. Two bands were formed; one consisted of *meso*benzanthrone (1·06 g.), the other was orange and less mobile. Elution of the second band with hot chlorobenzene gave a solid (0·09 g.), and this after repeated crystallisation from chlorobenzene afforded yellow prisms, m. p. 421—422° (Found : C, 87·7; H, 4·0. Calc. for $C_{34}H_{16}O_2$: C, 89·1; H, 3·9%) not depressed on admixture with authentic 3 : 3′-di*meso*benzanthronyl [yellow prisms; m. p. 420—421° (Found : C, 88·3, 88·0; H, 4·0, 3·8. Calc. for $C_{34}H_{16}O_2$: C, 89·1; H, 3·9%); Lüttringhaus and Neresheimer (*Annalen*, **1929**, **473**, 259) record m. p. 412—414°] prepared from 3-bromo*meso*benzanthrone. The identity of the two samples of 3 : 3′-di*meso*benzanthronyl was confirmed by a comparison of the light absorption of their 0·001% solutions in concentrated sulphuric acid. Values of 10^{-4} ε are given in parentheses, those for the product from 3-bromo-*meso*benzanthrone being given first : $\lambda_{max.}$ 206 (7·40, 6·95), 247 (6·56, 6·67), 375 (3·73, 3·67), 430 (1·78, 1·79), 543—544 (3·22, 3·44) mμ. $\lambda_{min.}$ 228 (5·01, 4·95), 279 (0·89, 0·82), 401—402 (1·25, 1·19), 454—455 (0·76, 0·76) mμ.

On being heated alone for 5 hr. at 290—320°, *meso*benzanthrone remained almost unchanged and no 3 : 3′-di*meso*benzanthronyl was formed.

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